# Fast Numerical Evaluation of Periodic Solutions for a Class of Nonlinear Systems and Its Applications for Parameter Estimation Problems

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**Abstract.** Fast numerical evaluation of forward models is central for a broad range of inverse problems. Here we propose a method for deriving computationally efficient representations of periodic solutions of parameterized systems of nonlinear ordinary differential equations. These representations depend on parameters of the system explicitly, as quadratures of parameterized computable functions. The method applies to systems featuring both linear and nonlinear parametrization, and time-varying right-hand side. In addition, it opens possibilities to invoke scalable parallel computations and suitable function approximation schemes for numerical evaluation of solutions for various parameter values. Application of the method to the problem of parameter estimation of nonlinear ordinary differential equations is illustrated with a numerical example for the Morris–Lecar system.

**Keywords:** Parameter estimation, Nonlinear Parametrization, Adaptive observers, Time-varying systems.

## 1 Introduction

The problem of state and parameter estimation of systems of ordinary differential equations (ODEs) has been in the focus of attention for many decades. Many frameworks for addressing this problem have been developed to date, including but not limited to shooting methods [6], sensitivity functions [1], splines [29] and adaptive observers [3], [18], [4], [10], [28], [26] (see also [16], [24] for system-identification take on the problem).

Notwithstanding significant progress in this area in both theoretical and applied directions, there is a fundamental yet practical issue with this problem affecting further progress. The issue is that, in general, expressing state variables of systems of ordinary differential equations as explicit *known functions* of

parameters and initial conditions or their quadratures is an challenging mathematical problem. Thus sequential numerical approximation of solutions over time is typically involved in the estimation process. The problem, however, is that this process is slow and does not scale well with computational resources available. At the same time there are problems such as e.g. real-time estimation of kinetic parameters of neural membranes [23] that do require fast estimation of model parameters. Hence new approaches are needed.

Here we provide a method enabling us to address the above fundamental challenges for a class of systems with nonlinear parameterziation. The main idea of the method is to present an observed quantity as an integral that is explicitly a) computable and b) explicitly dependent on the parameters entering the original ODE model nonlinearly. Doing so enables to benefit from computational advantages of prefix sum algorithms [5] and thus alleviate the issues of scalability and real-time. Our preliminary work in this direction [27, 19] showed that employing the tools of adaptive observer design [18, 11] provides a feasible solution for a relevant class of systems. We demonstrate that further improvement might be achieved by replacing certain integrals with their approximations by e.g. Radial Basis Functions [22].

The contribution is organized as follows. Section 2 specifies main technical assumptions and details mathematical statement of the problem. Section 3 presents main ingredients of the method. In Section 4 we discuss these results in relation to the possibility of replacing some integrals in the representation with their approximations. Section 5 presents a numerical example, and Section 6 provides a brief conclusion.

## 2 Problem Formulation

Throughout the paper the following notational agreements are used. Symbol $\mathbb{R}$ denotes the field of real numbers, and $\mathbb{R}^n$ stands for the $n$-dimensional real space. Let $x \in \mathbb{R}^n$, then $\|x\|$ is the Euclidean norm of $x$: $\|x\| = \sqrt{x_1^2 + \cdots + x_n^2}$. $\mathcal{C}^r$ denotes the space of continuous functions which are differentiable at least $r$ times. By $L_\infty^n[t_0, T]$ or, when $n$ is clear from the context, $L_\infty[t_0, T]$ we denote the space of all functions $f : [t_0, T] \to \mathbb{R}^n$ such that $\|f\|_{\infty,[t_0,T]} = \sup_{t\in[t_0,T]} \|f(t)\| < \infty$, and $\|f\|_{\infty,[t_0,T]}$ stands for the $L_\infty^n[t_0, T]$ norm of $f(\cdot)$.

### 2.1 System Definition

Consider the following class of nonlinear systems

$$\begin{array}{l} \dot{x} = F(y,t)x + \Psi(y,t)\theta + g(y,\lambda,t) \\ y(t) = C_1^T x;\ x(t_0) = x_0, \end{array} \tag{1}$$

where $x \in \mathbb{R}^n$ and $y \in \mathbb{R}$ are the state and the output of the system, respectively, $F(y,t) \in \mathbb{R}^{n\times n}$ is a known matrix dependent on $y$ and $t$; $\lambda \in \Omega_\lambda$, $\Omega_\lambda \subset \mathbb{R}^p$, $\theta \in \Omega_\theta$, $\Omega_\theta \subset \mathbb{R}^m$ are parameters, and $C_1 \in \mathbb{R}^n$: $C_1 = \mathrm{col}(1, 0, \cdots, 0)$. With regards to the sets $\Omega_\theta$, $\Omega_\lambda$, they are allowed to be arbitrary subsets of $\mathbb{R}^m$ and

$\mathbb{R}^p$, respectively. Unless stated otherwise, no other prior knowledge about the sets $\Omega_\theta$, $\Omega_\lambda$ is assumed.

Other technical assumptions are detailed in Assumption 1 below.

**Assumption 1** *The following properties hold for* (1)*:*

1. *the solution of* (1) *is defined for all* $t \geq t_0$*, and it is* $T$*-periodic,* $T > 0$*;*
2. *the function* $F$ *is continuous, bounded, and* $F(y(\cdot), \cdot)$ *is* $T$*-periodic;*
3. *exact values of parameters* $\lambda$ *and* $\theta$ *are unknown;*
4. *the values of* $y(t)$ *for* $t \in [t_0, t_0 + T]$ *are available and known;*
5. *the function* $\Psi : \mathbb{R} \times \mathbb{R} \to \mathbb{R}^{n \times m}$ *is such that* $\Psi(y(\cdot), \cdot)$ *is* $T$*-periodic and is in* $L_\infty[t_0, \infty) \cap \mathcal{C}^0$*;*
6. *the function* $g : \mathbb{R} \times \mathbb{R}^p \times \mathbb{R} \to \mathbb{R}^n$ *is such that* $g(y(\cdot), \lambda, \cdot)$ *is* $T$*-periodic and is in* $L_\infty[t_0, \infty) \cap \mathcal{C}^1$ *for all* $\lambda \in \Omega_\lambda$*;*
7. *the observability Gramian matrix*

$$G(T, t_0) = \int_{t_0}^{t_0+T} \Phi_A(s, t_0) C C^T \Phi_A^T(s, t_0) ds, \; C = \mathrm{col}(1, 0, \ldots, 0),$$

*where* $\Phi_A(t, t_0)$*, is the normalized (i.e.* $\Phi_A(t_0, t_0) = I_{n+m}$*) fundamental solution matrix of*

$$\begin{aligned} \dot{x} &= A(y(t), t)x, \\ A(y(t), t) &= \begin{pmatrix} F(y(t), t) & \Psi(y(t), t) \\ 0 & 0 \end{pmatrix}, \end{aligned} \tag{2}$$

*is of full-rank, i.e* $\mathrm{rank}(G(T, t_0)) = n + m$*.*

The class of equations (1) accommodates a broad set of technical and natural systems ranging from models of [2], dynamics of populations [14], and neural membranes [20]. In case the solutions are periodic it also may, after suitable modifications [27], include systems

$$\begin{aligned} \dot{x} &= F(y, t)x + \Psi(y, t)\theta + g(y, q, \lambda, t) \\ \dot{q} &= \upsilon(y, \lambda, t)q + \omega(y, \lambda, t) \\ y &= C_1^T x; \; x(t_0) = x_0, \; q(t_0) = q_0, \end{aligned} \tag{3}$$

in which the functions $\upsilon(y(\cdot), \lambda, \cdot)$, $\omega(y(\cdot), \lambda, \cdot)$ are continuous.

For notational convenience (cf. [25]), in what follows, we will combine the state variable $x$ and parameters $\theta$ entering the right-hand side of (1) linearly into a single variable $\chi$ and rewrite the system accordingly:

$$\dot{\chi} = A(y, t)\chi + \begin{pmatrix} g(y, \lambda, t) \\ 0 \end{pmatrix}, \; y(t) = C^T \chi, \; \chi(t_0) = \chi_0. \tag{4}$$

In (4) $\chi = (x, \theta)$ is the combined state vector, matrix $A(y, t)$ is defined as in (2), and $C \in \mathbb{R}^{n+m}$ is $C = \mathrm{col}(1, 0, \cdots, 0)$. Let us now proceed with the formal definition of the problem considered in this contribution.

### 2.2 Problem Statement

Consider system (4) and suppose that the values of $y(t)$ for $t \in [t_0, t_0 + T]$ are known and available *a-priori*. These values will depend on the parameters $\lambda$ and initial condition $\chi_0$ which themselves are assumed to be *unknown*. The question is if there exists an operator $\mathcal{F}$ mapping $y(\cdot)$ over $[t_0, t_0 + T]$ into an efficiently computable quantity that does depend on the parameters $\lambda$ explicitly?

In particular, we are seeking for an $\mathcal{F}(\lambda, [y], t)$ such that

$$\begin{aligned} &C^T \chi(t; t_0, \chi_0, \lambda) = \mathcal{F}(\lambda, [y], t), \ \forall\ t \in [t_0, t_0 + T], \ \lambda \in \Omega_\lambda, \\ &\mathcal{F}(t, \lambda, [y]) = \pi(t, \lambda, [y]) + \int_{t_0}^{t} p(\tau, \lambda, y(\tau), [y]) d\tau, \end{aligned} \tag{5}$$

in which the functionals $\pi$ and $p$ are known and computable, e.g. in quadratures. The functionals $\pi$, $p$ must not depend on $\chi_0$ as a parameter, but nevertheless have to ensure the required representation (5).

In what follows, (Theorem 2 in Section 3) we demonstrate that finding the required representations $\mathcal{F}(\lambda, [y], t)$ is possible, subject to some mild technical conditions largely contained in Assumptions 1, 2. When such a representation is found one can employ numerous off-line numerical optimisation techniques to infer the values of $\lambda$, $\theta$, and initial conditions from the values of $y$ in the interval $[t_0, t_0 + T]$. We will illustrate this step with an example in Section 5 in which the Nelder–Mead algorithm [21] will be used for this purpose.

## 3 Observer-based Explicit Parametrized Representations of Periodic Solutions

The problem of existence of representations (5) in the context of parameter estimation is hardly viable without assessing parameter identifiability [9] of (4). The corresponding sufficient conditions are derived below.

### 3.1 Indistinguishable Parametrizations of (4)

We begin with the following technical lemma [19] (cf. [28]).

**Lemma 1.** *Consider the following class of system*

$$\dot{\chi} = A_0(t)\chi + u(t) + d(t), \ y = C\chi, \ \chi(t_0) = \chi_0, \quad \chi_0 \in \mathbb{R}^\ell, \tag{6}$$

*where*

$$A_0(t) = \left(\begin{array}{c|c} \alpha_1(t) & \beta_2(t) \ \ \beta_3(t) \ \ \cdots \ \beta_\ell(t) \\ \hline \alpha_2(t) & \\ \vdots & \quad A_0^*(t) \\ \alpha_\ell(t) & \end{array}\right) \text{ and } u, d, \alpha : \mathbb{R} \to \mathbb{R}^\ell,\ \beta : \mathbb{R} \to \mathbb{R}^{\ell-1},$$

$u \in \mathcal{C}^1$, $d, \alpha, \beta \in \mathcal{C}, \alpha = \mathrm{col}(\alpha_1(t), \alpha_2(t), \ldots, \alpha_\ell(t))$, $\beta = (\beta_2(t), \beta_3(t), \ldots, \beta_\ell(t))$, *and assume that solutions of* (6) *are globally bounded in forward time.*

*Let, in addition:*

1. *$u, \dot{u}, d, \alpha, \beta$ be bounded:* $\max\{\|u(t)\|, \|\dot{u}(t)\|\} \leq B$, $\|d(t)\| \leq \triangle_\xi, \|\alpha(t)\| \leq M_1, \|\beta(t)\| \leq M_2$ *for all* $t \geq t_0$.

2. *there exist a* $b : \mathbb{R} \to \mathbb{R}^{\ell-1}, b \in \mathcal{C}, \|b(t)\| \leq M_3$ *such that the zero solution of the system*

$$\dot{z} = \Lambda(t)z, \qquad \Lambda(t) = A_0^*(t) - b(t)\beta(t),$$

*is uniformly exponentially stable, and let* $\Phi_\Lambda(t, t_0)$ *be the corresponding fundamental solution:* $\Phi_\Lambda(t_0, t_0) = I_\ell$.

*Then the following statements hold:*

1. *If the solution of* (6) *is globally bounded for all* $t \geq t_0$ *then, for* $T$ *sufficiently large, there are* $k_1, k_2 \in \mathcal{K}$ *:*
$\|y(t)\|_{\infty,[t_0,t_0+T]} \leq \epsilon \Rightarrow \exists\ \ t'(\epsilon, x_0) \geq t_0$*:* $\|h(\tau) + u_1(\tau)\|_{\infty,[t',t_0+T]} \leq k_1(\epsilon) + k_2(\triangle_\xi)$*, where* $h(t) = \beta(t)z$,

$$\begin{array}{l} \dot{z} = \Lambda(t)z + Gu, \\ G = \begin{pmatrix} -b(t) & I_{\ell-1} \end{pmatrix}, \quad z(t_0) = 0, \end{array} \tag{7}$$

2. *If* $d(t) \equiv 0$*, then* $y(t) = 0$ *for all* $t \in [t_0, t_0+T]$ *implies existence of* $P \in \mathbb{R}^{\ell-1}$*:*

$$\beta(t)\Phi_\Lambda(t, t_0)P + h(t) + u_1(t) = 0 \tag{8}$$

*for all* $t \in [t_0, t_0 + T]$.

According to Lemma 1 the set of parameters:

$$\mathcal{E}(\lambda) = \{\lambda' \in \mathbb{R}^p |\ \exists\ p \in \mathbb{R}^{\ell-1} :\ \eta(t, p, \lambda', \lambda) = 0,\ \forall t \in [t_0, t_0 + T]\} \tag{9}$$

where

$$\begin{array}{l} \eta(t, p, \lambda', \lambda) = \beta(t)\Phi_\Lambda(t, t_0)p + g_1(y(t), \lambda', t) - g_1(y(t), \lambda, t) + \\ \beta(t) \displaystyle\int_{t_0}^{t} \Phi_\Lambda(t, \tau)G(\tau) \begin{pmatrix} g(y(\tau), \lambda', \tau) - g(y(\tau), \lambda, \tau) \\ 0 \end{pmatrix} d\tau, \end{array}$$

and $\Lambda$ is defined as in (7), contains parameters $\lambda'$ producing measurements $y(t) = C^T\chi(t; t_0, \chi_0, \lambda')$ that are indistinguishable from $C^T\chi(t; t_0, \chi_0, \lambda)$ on the interval $[t_0, t_0 + T]$. If the set $\mathcal{E}(\lambda)$ contains more than one element then the system (4) may not be uniquely identifiable on $[t_0, t_0 + T]$. Notwithsdanding existence and possible utility of systems that are not uniquely identifiable, we will nevertheless focus on systems (4) that are uniquely identifiable on $[t_0, t_0+T]$. Thus we assume that the following holds:

**Assumption 2** *For every* $\lambda \in \Omega_\lambda$*, the set* $\mathcal{E}(\lambda)$ *consists of just one element.*

### 3.2 Auxiliary Observer in the Differential Form

In addition to (4) consider the following *auxiliary* system:

$$\begin{aligned}\dot{\hat{\chi}} &= A(y(t),t)\hat{\chi} + \begin{pmatrix} g(y(t),\lambda',t) \\ 0 \end{pmatrix} - R^{-1}C(C^T\hat{\chi} - y), \\ \dot{R} &= -\delta R - A(y(t),t)^T R - RA(y(t),t) + CC^T \\ \hat{\chi}(t_0) &= \hat{\chi}_0 \in \mathbb{R}^{n+m},\ R(t_0) \in \mathbb{R}^{(n+m)\times(n+m)},\end{aligned} \tag{10}$$

where $\hat{\chi} \in \mathbb{R}^{n+m}$ is the observer's state, $R(t_0)$ is a positive-definite symmetric matrix, and $\delta \in \mathbb{R}_{>0}$ is a positive parameter. Solutions of (10) are defined for all $t \geq t_0$ (see items (1), (2) in Assumption 1), and hence, [11], $R(t)$ is given by

$$\begin{aligned}R(t) = e^{-\delta(t-t_0)}\Phi_A(t_0,t)^T R(t_0)\Phi_A(t_0,t) + \\ \int_{t_0}^{t} e^{-\delta(t-s)}\Phi_A(s,t)^T CC^T\Phi_A(s,t)ds.\end{aligned} \tag{11}$$

It is clear that $R(t)$ is non-singular for all $t \geq t_0$, symmetric, and positive-definite. Furthermore, if the value of the parameter $\delta > 0$ is chosen so that

$$\|e^{-\delta(t-t_0)/2}\Phi_A(t_0,t)\| \leq De^{-a(t-t_0)},\ a > 0, \tag{12}$$

then $R(t)$ is bounded. In what follows the following additional assumption is instrumental:

**Assumption 3** *There exist $t_1 \geq t_0$ and $\alpha(\delta) > 0$ such that*

$$\phi(t,\delta) = \int_{t_0}^{t} e^{-\delta(t-s)}\Phi_A(s,t)^T CC^T\Phi_A(s,t)ds \geq \alpha(\delta)I_{n+m}$$

*for all $t \geq t_1$.*

The next theorem specifies asymptotic behaviour of the observer system (10) (adapted from [11]).

**Theorem 1.** *Consider (10) and suppose that $\delta > 0$ be chosen so that both (12) and Assumption 3 hold, and $\lambda' = \lambda$. Then there exists a $t_2 \geq t_0$, such that:*

$$\|\hat{\chi}(t;\hat{\chi}_0) - \chi(t;\chi_0)\| \leq ke^{-\delta(t-t_0)}$$

*for all $t \geq t_2$, where $k$ is a constant dependent on $\delta$, $t_0$, $\chi_0$ and the initial state $\hat{\chi}_0$ of the observer system* (10)*.*

Theorem 1 states the variable $\hat{\chi}(t)$ asymptotically tracks $\chi(t)$, and that the difference between the two converges to zero exponentially. Here, however, we are interested in establishing finite-time relationships (5). To do so we need another technical result establishing sufficient conditions for the existence of unique periodic solutions of $R$. The result is provided in Lemma 2 [19].

**Lemma 2.** *Consider (10) with $A(y(t),t)$ being $T$-periodic. Then, for sufficiently large $\delta > 0$, there exists a unique symmetric $R(t_0)$ ensuring that the function $R(t)$ defined by* (11) *is $T$-periodic. If, in addition, (12) and Assumption 3 hold then $R(t_0)$ is positive-definite.*

### 3.3 Integral Parametrization of Periodic Solutions of (4)

For notational convenience, let us rewrite auxiliary observer equations (10) as:

$$\begin{aligned}\dot{\hat{\chi}} &= (A(t) - R^{-1}CC^T)\hat{\chi} + \begin{pmatrix} g(y(t), \lambda', t) \\ 0 \end{pmatrix} + R^{-1}Cy(t) \\ \dot{R} &= -\delta R - A(y(t), t)^T R - RA(y(t), t) + CC^T \\ \hat{\chi}(t_0) &= \hat{\chi}_0 \in \mathbb{R}^{n+m},\ R(t_0) \in \mathbb{R}^{(n+m)\times(n+m)},\end{aligned} \tag{13}$$

and additionally consider dynamics of the linear part of the first equation:

$$\xi = \left( A(y(t), t) - R^{-1}(t)CC^T \right) \xi. \tag{14}$$

Let $\Phi(t, s)$ be the normalized fundamental solution matrix of (14), i.e. $\Phi(t, t) = I_{n+m}$ and $\Phi(s, t) = \Phi(t, s)^{-1}$.

**Theorem 2.** *Consider system (13) and suppose that Assumptions 1 and 2 hold. In addition, suppose that condition (12) hold and the values of $\delta$ and the initial condition $R(t_0)$ in (13) are chosen such that $R(t) > 0$ is $T$-periodic.*

*Consider the function $\hat{y} : \mathbb{R}^p \times \mathbb{R} \to \mathbb{R}$:*

$$\begin{aligned}\hat{y}(\lambda', t) = C^T \big(&\Phi(t, t_0)\hat{\chi}_0 + \\ &\int_{t_0}^{t} \Phi(t, \tau) \left( R^{-1}(\tau)Cy(\tau) + \begin{pmatrix} g(y(\tau), \lambda', \tau) \\ 0 \end{pmatrix} \right) d\tau\big)\end{aligned} \tag{15}$$

*where*

$$\begin{aligned}\hat{\chi}_0 = (I_{n+m} - \Phi(t_0 + T, t_0))^{-1} &\int_{t_0}^{t_0+T} \Phi(t_0 + T, \tau) \times \\ &\left( R^{-1}(\tau)Cy(\tau) + \begin{pmatrix} g(y(\tau), \lambda', \tau) \\ 0 \end{pmatrix} \right) d\tau.\end{aligned} \tag{16}$$

*Then*

$$\hat{y}(\lambda', t) = C\chi(t; t_0, \chi_0, \lambda)\ \forall\ t \in [t_0, t_0 + T] \Leftrightarrow \lambda = \lambda'.$$

The proof can be found in [19].

## 4 Discussion

One of the immediate computational advantages of the method is that the proposed integral representations offer a possibility to employ parallel calculations. In addition, the method offers reduction of dimensionality of the problem due to incorporating linearly parameterized part of the model into internal variables of the proposed representations. These internal variables are uniquely determined by parameters entering the model nonlinearly and are computed as a part of the representation.

In what follows we will show that further computational improvements might be possible and are practically viable (as illustrated with an example) if certain variables in the representations are replaced by their reasonable sparse Radial Basis Function approximations.

One of the key steps justifying incorporation of relevant class of equations specified by (3) into the setting focusing on (1) was an assumption that the variable $q(t; q_0, \lambda, y)$ is expressible as a known function of parameters, initial conditions, and $t$. For example, if $q$ relates to a single first-order equation then such function can be computed as follows:

$$\begin{aligned} q(t; q_0, \lambda, y) = e^{\int_{t_0}^{t} \upsilon(y(\tau),\lambda,\tau)d\tau} q_0 + e^{\int_{t_0}^{t} \upsilon(y(\tau),\lambda,\tau)d\tau} \times \\ \int_{t_0}^{t} e^{-\int_{t_0}^{\tau} \upsilon(y(s),\lambda,s)ds} \omega(y(\tau),\lambda,\tau)d\tau \\ q_0 = (1 - e^{-\int_{t_0}^{t_0+T}(\upsilon(y(s),\lambda,s)ds})^{-1} \int_{t_0}^{t_0+T} e^{-\int_{z}^{t}(\upsilon(y(s),\lambda,s))ds} \omega(y(z),\lambda,z)dz. \end{aligned} \tag{17}$$

If the original problem is governed by (3) then availability of $q(t; q_0, \lambda, y)$ is required in our explicit parameter-dependent representation. One way to resolve the problem is to numerically evaluate all integrals involved. This, however, may not always be optimal. An alternative could be to use computationally efficient approximations of $q(t; q_0, \lambda, y)$ instead.

A possible class of approximations is the class of Radial Basis Functions (RBF) which are known to be efficient for approximating scattered datasets [7]. Recall that Radial Basis Functions are those functions that exhibit radial symmetry, that is, may be seen to depend only (apart from some known parameters) on the distance $r = \|X - X_c\|$ between the centre of the function, $X_c$, and a generic point $X$. These functions may be generically represented in the form $\phi(r)$, where the function $\phi$ is a real-valued function of a real non-negative argument. The functions $\phi$ may be both globally or compactly supported, and Table 1 presents some relevant examples. The Gaussian and the inverse multiquadric are positive definite, so that the matrices which arise in interpolation problems are invertible. The other functions are conditionally positive definite, and a polynomial needs to be appended in general so that the interpolation problem is well-posed [7].

| Infinitely smooth RBFs | Functional Form, $\phi(r)$ | Parameters |
|---|---|---|
| Polyharmonic Spline | $r^k$ | $k > 0, k \notin 2\mathbb{N}$ |
| Gaussian | $e^{-(\alpha r)^2}$ | $\alpha > 0$ |
| Multiquadric(MQ) | $(1 + \alpha^2 r^2)^{k/2}$ | $k > 0, k \notin 2\mathbb{N}, \alpha > 0$ |
| Inverse multiquadric | $(1 + \alpha^2 r^2)^{k/2}$ | $k < 0, k \notin 2\mathbb{N}, \alpha > 0$ |

**Table 1.** Some commonly used radial basis functions. Parameter $\alpha$, called "local shape parameter", controls the shape of the radial basis function.

Let $X \in \mathbb{R}^d$ be a vector accommodating relevant measurement parameters, i.e. $t$ and $\lambda$. In other words, $X = (t, \lambda)$. Consider $X_c = \{X_{c_1}, X_{c_2}, \cdots, X_{c_M}\}$. The centres $X_c$ could be selected from the given data samples or derived via

clustering algorithms. Let

$$S(X) = \sum_{j=1}^{M} \omega_j \phi(\|X - X_{c_j}\|) + p(X),\ X \in \mathbb{R}^d, \tag{18}$$

where $p$ is a polynomial, be an RBF approximation of $q(t; q_0, \lambda, y)$ or simply $q(t, \lambda)$, where $\omega_j$ are unknown coefficients that need to be determined. The polynomial $p$ is appended when $\phi$ is not positive definite. It is well-known that, for a broad range of $\phi(\cdot)$, any continuous function on a bounded domain can be approximated by sums (18) with arbitrary accuracy in $L_p$-norm, $p > 1$, subject to the choice of parameters $X_{c_j}$, $\omega_j$, and $M$ [22].

The following heuristics is proposed to replace repeat evaluations (17) of $q(t, \lambda)$ with their RBF approximations in a generic optimisation routine for inferring the values of $\theta$ and $\lambda$.

**Algorithm 1** *[Parameter inference with approximated variables]*

1. *Initialisation: set $\hat{\lambda}$ as an initial guess of $\lambda$.*
2. *A set of $M$ samples $X_i = (t_{n_i}, \lambda_{m_i})$ is randomly drawn from a relevant domain or chosen in accordance with some pre-defined process. The domain, in general, may depend on $\hat{\lambda}$.*
3. *Group spatially close points using a suitable clustering algorithm (e.g. [15, 8, 13, 12]), and set the centres $X_{cj}$ as the centres of these clusters.*
4. *Determine parameters $\omega_j$ in (18) as the minimizer of $\sum_{i=1}^{N}(S(X_i) - q(t_i, \lambda_i))^2$, $N > 0$. Note that adjustments of the shape parameter, $\alpha$, might be needed to ensure good approximation.*
5. *Using representation* (15) *and approximant (18) define:*

$$\begin{aligned} \tilde{y}(\hat{\lambda}, t) &= F(t, t_0, \theta, \hat{\lambda}, \hat{q}(\hat{\lambda}, t)) \\ \hat{q}(\hat{\lambda}, t) &= \textstyle\sum_{k=1}^{M} \omega_k \phi(\|(t, \hat{\lambda}) - (t_{c_k}, \lambda_{c_k})\|). \end{aligned} \tag{19}$$

   *The function $\tilde{y}(\hat{\lambda}, t)$ is an approximation of $\hat{y}(\hat{\lambda}, t)$.*
6. *Use $\tilde{y}(\hat{\lambda}, t)$, to produce a refined guess of $\hat{\lambda}$ and return to Step 1 if required.*

In the next section we illustrate an application the method (with and without Algorithm 1) to the problem of parameter estimation for the Morris–Lecar system.

## 5 Example

### 5.1 Direct Application of the Method

Consider the following simple point model of neural membrane activity [20]:

$$\begin{aligned} \dot{x} &= g_{Ca} m_\infty(x)(x - E_{Ca}) + g_K q(x + E_K) + g_L(x + E_L) + I \\ \dot{q} &= -\tau(x)^{-1} q + \tau(x)^{-1} \omega_\infty(x),\ y = x, \end{aligned} \tag{20}$$

where

$$m_\infty(x) = 0.5\left(1+\tanh\left(\tfrac{x-V_1}{V_2}\right)\right),\ \omega_\infty(x) = 0.5\left(1+\tanh\left(\tfrac{x+V_3}{V_4}\right)\right)$$
$$\tau(x) = T_0/\left(\cosh\left(\tfrac{x+V_3}{2V_4}\right)\right).$$

Here $x$ is the measured voltage, $q$ is the recovery variable. Parameters $E_{Ca}, E_K, E_L$ are the Nernst potentials of which the nominal values are assumed to be *known*: $E_{Ca} = 55.17, E_K = -110.14, E_L = 49.49$; other parameters may vary from one cell to another and thus are considered *unknown*.

Assume that the model operates in the oscillatory regime which corresponds to periodic solutions of (20). For practically relevant values of $T_0, V_3, V_4$ and measurements $x(\cdot)$ the integral $\int_{t_0}^{t_0+T}\tau(x(s))^{-1}ds > 0$, where $T$ is the period of oscillations. Given that $x(\cdot)$ is $T$-periodic, the variable $q$ can be expressed as:

$$q(t) = e^{-\int_{t_0}^{t}\tau(x(s))^{-1}ds}q_0 + \int_{t_0}^{t} e^{-\int_{z}^{t}\tau(x(s))^{-1}ds}\tau(x(z))^{-1}\omega_\infty(x(z))dz$$
$$q_0 = \left(1-e^{-\int_{t_0}^{t}\tau(x(s))^{-1}ds}\right)^{-1}\int_{t_0}^{t_0+T} e^{-\int_{z}^{t_0+T}\tau(x(s))^{-1}ds}\tau(x(z))^{-1}\omega_\infty(x(z))dz.$$

Denoting $g(t,\lambda,[y]) = g_{Ca}m_\infty(x)(x-E_{Ca}) + g_K q(x+E_K)$, $\Psi(t,y) = (y(t),1)$, and combining parameters as $\theta = (g_L, I)$, $\lambda = (V_1, V_2, V_3, V_4, T_0, g_{Ca}, g_K)$ we can rewrite (20) in the form of equation (4) with

$$A(y(t),t) = \begin{pmatrix} 0 & y(t) & 1 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

For this system and chosen nominal parameter values, the period of oscillations is $T = 15.1692$. For convenience, the integration interval was et as $[0, 15.1692]$. Numerical evaluations of integrals and solutions of all auxiliary differential equations have been performed on equi-spaced grids with the step size of 0.0002.

According to Theorem 2, explicit parameter-dependent representation of the observed quantity, $\hat{y}(\lambda,t)$, is defined by (15), where $C = (1,0,0)$, $\chi = \mathrm{col}(x,\theta)$, and the fundamental solution $(3\times3)$-matrices $\Phi(t,t_0)$ and $\Phi_A(t,t_0)$ are computed for the linear systems $\dot{\chi} = (A(y(t),t) - R^{-1}(t)CC^T)\chi$, $\dot{R} = -\delta R - A(y(t),t)^T R - RA(y(t),t) + CC^T$, and $\dot{\chi} = A(y(t),t)\chi$, respectively, by the Improved Euler method for $t \in [0, 15.1692]$. The value of $\delta$ was set as $\delta = 2$, and numerical approximations of matrices $\Phi_A(t,t_0)$ were used to compute the matrices $R(t)$ in accordance with equation (11). The value of $R(t_0)$ in (11) was so that $R(t)$ is periodic (see Lemma 2).

Figure 1 shows the relative error, $e(t) = (\hat{y}(\lambda,t) - y(t))/\|y\|_{\infty,[t_0,t_0+\infty]}$, between the proposed numerical representation (15) and simulated $y(t)$ (Runge–Kutta, step size 0.0002) for nominal parameter values.

The parameterized representations were later used, in combination with the Nelder–Mead algorithm [21] to recover the values of parameters $\lambda$ and $\theta$. Results of the estimation process after 3000 steps are shown in Table 2. The process took less than 10 minutes on a standard PC in Matlab R2015a.

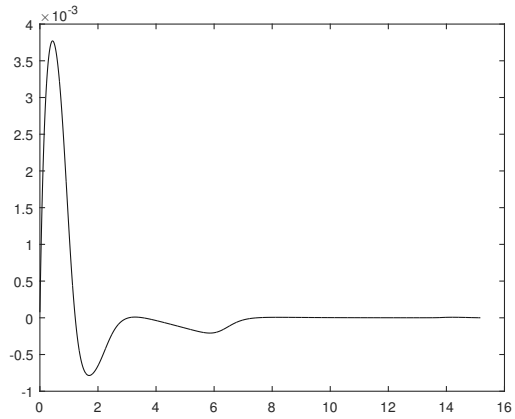


**Fig. 1.** Relative error $e(t) = (\hat{y}(\lambda, t) - y(t))/\|y\|_{\infty,[t_0,t_0+\infty]}$ as a function of $t$.

**Table 2.** True (first row) and Estimated (second row) of $\lambda$ and $\theta$, and the value of $x_0$

Vector $\lambda = (V_1, V_2, V_3, V_4, T_0, g_{Ca}, g_K)$

| $V_1$ | $V_2$ | $V_3$ | $V_4$ | $T_0$ | $g_{Ca}$ | $g_K$ |
|---|---|---|---|---|---|---|
| -1 | 15 | -10 | 14.5 | 3 | -1.1 | -2 |
| -0.999 | 14.999 | -10.000 | 14.500 | 3.000 | -1.100 | -2.000 |

Vector $\theta = (g_L, I)$ and $x_0$

| $g_L$ | $I$ | $x_0$ |
|---|---|---|
| -0.5 | 10 | 21.96388 |
| -0.49982 | 9.99345 | 21.96166 |

**Table 3.** Time for 1000 evaluations of $y$

| Eq. (15) | Improved Euler method | Ratio |
|---|---|---|
| 2.21311 minutes | 10.43818 minutes | 4.71652 |

To assess potential computational advantage of the proposed approach we compared the time required for 1000 evaluations of $y(t)$ in Matlab a) expressed as in (15) and b) computed by the Improved Euler method over the interval $[t_0, t_0 + T]$. The parameter values for both cases were kept identical and did not change from one trial to the other. The results are summarized in Table 3.

### 5.2 The Method with RBF Approximation of $q$

To show feasibility of RBF approximations in this problem we repeated the experiment above but this time with the variable $q$ replaced with its RBF approximation inside the optimisation routine (Nelder–Mead). To produce such approximations we followed steps of Algorithm 1. As the RBF kernel we used the Gaussian function. This transforms (18) into

$$S_q(X) = \sum_{j=1}^{M} \omega_j e^{-(\alpha \|X - X_{c_j}\|)^2}. \tag{21}$$

Note that the variable $q$ depends only on 3 components of the vector $\lambda$, i.e. $T_0$,$V_3$, and $V_4$. And hence all steps of the algorithm related to approximation apply to these 3 relevant components and the variable $t$ only. We considered an extremely sparse setting, in which each of the three parameters have been sampled at 2 points per each relevant sample of $t$. The values of $t$ where chosen from the grid of 0.002-spaced points in $[0, 15.1692]$ ($N = 7584$ points in the grid). The shape parameter $\alpha$ was set to 0.0222. To see how well $S_q(t_i, \hat{\lambda})$ approximates $q(t_i, \lambda)$ as a function of $t_i$ the following simple criterion has been used:

$$LS = \sum_{i=1}^{N} (q(t_i, \lambda) - S_q(t_i, \hat{\lambda}))^2. \tag{22}$$

In order to judge the efficiency of the approach we run the algorithm 1000 times and recorded empirical errors between $\lambda_i$ and their estimates $\hat{\lambda}_i$, and computed their $L_2$ distances as:

$$d(\nu) = \sqrt{\textstyle\sum_{i=1}^{7} (\lambda_i - \hat{\lambda}_i(\nu))^2}, \tag{23}$$

where $\nu = 1, \cdots, 1000$ is the number of the experiment. Initial guesses for $\lambda$ were selected randomly in the $n$-cube $[0, 1] + \lambda_i,\ i = 1, 2, \cdots, 7$, where $\lambda_i$ are the nominal values. Fig. 2 shows histograms of (22), (23) at the initial step of the algorithm. Fig. 3 shows histograms of the distributions of distances between $\lambda$ and $\hat{\lambda}$ and the least square errors (LS) after the application of Nelder–Mead method with Algorithm 1 used to approximate $q(t, \hat{\lambda})$. We observe a pronounced shift of the histograms to the left, where they concentrate around zero. This contrasts sharply with the initial distributions of errors seen in Fig.2.

As can be seen from these experiments, RBF approximation is a viable way to further improve scalability and potential of the method.

## 6 Conclusion

The work presented a method for computationally efficient and explicit parameter-dependent representation of periodic solutions of systems of nonlinear ODEs. The method is rooted in the ideas from adaptive observers theory and is an extension of our earlier work [27] in which linear part of the system was supposed

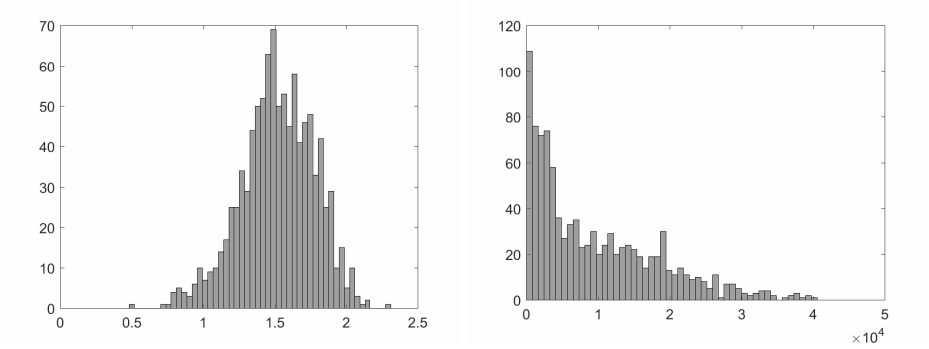


**Fig. 2.** Histograms of the distributions of $d(\nu),\ \nu = 1, \cdots, 1000$ (left panel), and least square errors $LS = \sum_{i=1}^{N}(q(t_i, \lambda) - S_q(t_i, \hat{\lambda}))^2$ (right panel) prior to any estimation.

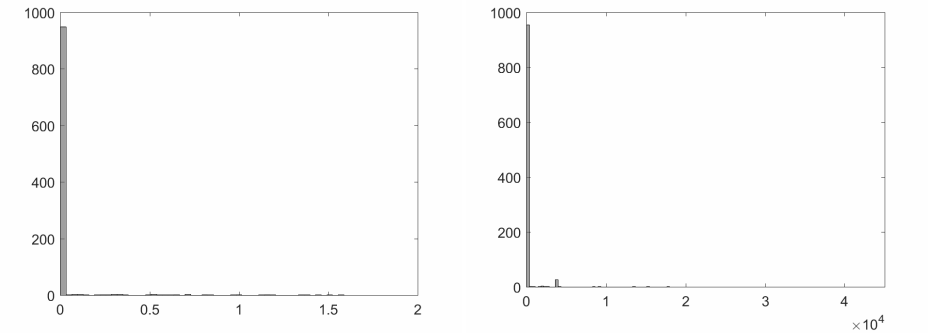


**Fig. 3.** Histograms of the distributions of $d(\nu),\ \nu = 1, \cdots, 1000$ (left panel) and $LS = \sum_{i=1}^{N}(q(t_i, \lambda) - S_q(t_i, \hat{\lambda}))^2$ (right panel) after optimisation.

to be time-invariant. Here we extended this result to systems with time-varying linear parts. Similar extension can be carried out for other observer structures, including e.g. [17], followed by replacement of condition (7) in Assumption 1 with the requirement of persistency of excitation of relevant terms.

The computational advantage of the method is due to the possible parallel implementation of calculations that the proposed representations offer. In addition to offering scalability and making use of parallel computations, the method offers reduction of dimensionality of the problem due to incorporating linearly parameterized part of the model into internal variables of the proposed representations. These internal variables are uniquely determined by parameters entering the model nonlinearly and are computed as a part of the representation.

An interesting possibility to further improve computational efficiency of the approach to a class of problems emerging in modelling dynamics of neural cells stems from invoking RBF approximations in place of certain integrals in the schemes. Viability of the approach in this setting has been demonstrated with a numerical example.

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