Parameter Range Reduction for ODE Models Using Monotonic Discretizations


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Abstract
This paper analyzes the effectiveness of various monotonic discretizations of an ODE in a parameter range reduction algorithm. Several properties of discretizations are given, and five classes of discretizations are defined for various step numbers \( s \). The range reduction algorithm that employs these discretizations is described. Using both analytical results based on the prototypical model \( x' = \lambda x \), and empirical results based on two more complicated models, it is shown that one particular class of discretizations (the A1OUT class) results in the tightest bounds on the parameters. This result is shown to be attributed to a certain characteristic value, \( A_0 \), of the discretization. Accumulation of these discretizations is also defined, and its usefulness in the range reduction algorithm is described.

Keywords: Parameter Range Reduction; Parameter Bounding; Monotonic Discretizations; Parameter Identification; Inverse Problems; Interval Analysis

1. Introduction
Consider a system of ordinary differential equations (ODEs) that models some physical or biological process and the parameter identification problem of determining appropriate model parameter values from time series data of the model variables. Specifically, consider models of the form
\[
x' = f(t, x, \lambda), \quad x \in \mathbb{R}^m, \quad \lambda \in \mathbb{R}^q,
\]
where the model parameters, \( \lambda \), are to be determined from time series data of the form \( S = \{(t_{\text{obs}}^n, x_{\text{obs}}^n)\}_{n=1}^N \). Denote the observation time interval as

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\[ I = [t_0^{\text{obs}}, t_N^{\text{obs}}], \] and, for a fixed \( \lambda \), denote the solution to (1) passing through the initial point \((t_0, \xi)\) as \( x(t, t_0, \xi, \lambda) \).

The typical way of identifying appropriate parameter values from such data involves the following steps:

1. Select an appropriate set of parameter values, \( \lambda \), and an initial point \((t_0, \xi)\)
2. Integrate the model equations to obtain \( x(t, t_0, \xi, \lambda) \)
3. Compute the error, typically \( \sum_{n=1}^{N} (x(t^n_{\text{obs}}, t_0, \xi, \lambda) - x^n_{\text{obs}})^2 \)
4. Repeat steps 1 to 3, selecting in step 1 to minimize the error

Depending on the size of the model, its stiffness, and the time span of the recorded data, integration of the model may represent a substantial computational effort. This effort is compounded by the number of iterations required for the algorithm to terminate. However, despite the computational effort of integration, the difficult task is the appropriate selection of a set of parameter values. It is possible that for a particular choice of the parameters integration of the differential equation across all of \( I \) is not even possible, in which case a better choice must be made somehow. In the first iteration, the parameter set must be selected from a potentially very large region of parameter space; an appropriate selection may not be obvious. This initial selection may affect not only the time required for the algorithm to terminate but also the final parameter values obtained, since the landscape of the error being minimized may have multiple local minima and/or large nearly flat regions in parameter space.

In subsequent iterations, selecting an appropriate set of parameter values (and initial values \( \xi \)) typically involves substantial further computation. Sometimes the update is determined by going downhill from the current location some distance \([1]\), or minimizing the error along a specific direction, or approximating the error function with a linear or quadratic function and minimizing this in a trust region around the current estimate \([2, 3]\). All of these update methods require information about the derivatives of the error with respect to the parameters and initial conditions and obtaining these derivatives necessarily requires further numerical integration. Derivative-free methods are also available \([4, 5]\), but these too can be computationally intense requiring many function evaluations.

Termination is determined by some combination of the following considerations: if the error is sufficiently small, if the recent parameter updates have not provided substantial improvement in the error, and if the amount of computing time has exceeded what is available. To be reasonably confident that a global minimizer of the error has been found, one typically needs to run this algorithm multiple times with different initial parameter sets. Sometimes this purpose is also achieved by allowing the updating step to not only go “downhill” but also occasionally explore far-off regions of parameter space. Various strategies used in global minimization may be applied to this problem \([6, 7]\), but regardless of the specific form of the above algorithm, the overall computational effort is typically large.

The final result of such a procedure is a point estimate in parameter space that (hopefully) is a best fit of the model to these particular data. Often the procedure provides little or no information about the sensitivity of the error to
changes in the parameters. In addition the recorded data likely are contaminated with noise, which may severely mask the underlying dynamics. Such a procedure also does not allow one to easily decide whether a particular model form is even appropriate for the phenomenon being recorded. A poor model form will simply manifest itself in a relatively large value for the minimum error. But quantifying “relatively” is difficult especially since a perfect model form applied to noisy data will also yield a relatively large minimum error value. Distinguishing these two cases may not be easy.

As an alternative to the above procedure, parameter bounding schemes have been used [8, 9, 10, 11, 12]. The emphasis of these have been the use of interval analysis and Taylor series constraint propagation to guarantee that portions of parameter space are either consistent or inconsistent with the data. Such procedures necessarily require known bounds on the data and employ validated numerical integration schemes [13] to determine whether the model solutions stay within these bounds. Although this paper discusses a parameter bounding scheme, it is not a scheme that uses validated techniques to produce guaranteed results. Instead, the point of view here is that whatever method is used to place bounds on noisy data is going to be somewhat arbitrary and so guaranteeing that the model solutions stay within these bounds is a stronger result than warranted.

The parameter range reduction scheme discussed in this paper was first introduced by Willms [14]. In this scheme, each of the $q$ parameters is given an initial range, which at worst is the whole real line, but in general is as small an interval as a priori information permits. The product of these ranges is a $q$-dimensional box in parameter space. The scheme reduces these ranges by chopping off slices of this box when it determines that the parameter values in that slice are inconsistent with the recorded data. The output of the scheme is a box or set of boxes enclosing the parameter sets that are not inconsistent with the data. Even if the volume of this output set is too large to meet the parameter identification precision desired by the user, it can be used to identify appropriate regions of parameter space from which to select initial parameter values to start a best point estimate algorithm of the type discussed above or as a set of starting boxes if one really wants to apply a guaranteed scheme. Typically, this parameter range reduction scheme rapidly reduces the size of the initial parameter box, resulting in knowledge about which parts of parameter space are inconsistent with the data and a much smaller remaining space through which to search for an optimal point estimate.

The parameter range reduction scheme uses certain monotonic discretizations of the differential equations. In [14] a class of discretizations called cumulative backward differentiation formulas was used. This paper introduces several other classes of monotonic discretizations, analyzes some of their properties, and compares their abilities to reduce parameter ranges using this scheme. Not all classes are equally effective, and a primary characteristic of a class is determined that correlates well with the class’s ability to reduce parameter ranges.

The remainder of this paper is organized as follows. Section 2 defines various classes of discretizations and gives several theoretical results about them. It also
introduces several different monotonic discretizations that will be analyzed later. The following section describes the parameter range reduction scheme in detail. Section 4 provides some analysis of the range reduction achieved by the different discretization classes when applied to some simple models. Empirical data on the performance of the scheme when applied to more complex models is given in Section 5, and the various discretizations are compared. A short conclusion ends the paper.

2. Discretizations

The types of discretizations of system (1) considered in this paper are of the form

$$F(t^0, h, s; x^0, x^1, \ldots, x^s, \lambda) := -\sum_{i=0}^{s} \alpha_i x^i + h \sum_{i=0}^{s} \beta_i f^i,$$

(2)

where $h > 0$ is the constant step size, $s \in \mathbb{N}$ is the number of steps in the discretization, each $x^i$, $0 \leq i \leq s$, is an independent variable in $\mathbb{R}^m$, $t^i = t^0 + i h$, and $f^i = f(t^i, x^i, \lambda)$. Superscripts are used for time indices and subscripts for spatial indices (vector components). The vector $x^i = [x^i_1, \ldots, x^i_m]^T$ then is an approximation to the solution of the ODE at time $t^i$, that is, to $x(t^i, t^0, \xi, \lambda) \in \mathbb{R}^m$. The discretization spans the time interval $[t^0, t^s]$. For brevity, when it is not necessary to emphasize the dependence of $F$ on its first three arguments, they are not written.

Discretizations of the form (2) are used in a number of ways. Setting $F = 0$ and imposing $\alpha_s = 1$ generates a linear multistep (LMS) method for numerical solution of the ODE (1). For example, $s = 1$, $\alpha_0 = -1$, $\alpha_1 = 1$, $\beta_0 = 1$, and $\beta_1 = 0$ is Euler’s method: $x^1 = x^0 + h f^0$. And $s = 2$, $\alpha_0 = 0$, $\alpha_1 = -1$, $\alpha_2 = 1$, $\beta_0 = -1/2$, $\beta_1 = 3/2$, and $\beta_2 = 0$ is the Adams-Bashforth order 2 method: $x^2 = x^1 + h \left(-\frac{1}{2} f^0 + \frac{3}{2} f^1\right)$. Discretizations are also used for numerical quadrature. If the function $f$ is independent of $x$, and if one sets $\alpha_0 = -1$, $\alpha_1 = \alpha_2 = \cdots = \alpha_{s-1} = 0$ and $\alpha_s = 1$, then $F = 0$ is an $(s + 1)$-point Newton-Cotes quadrature rule for the function $f(t, \lambda)$ from $t^0$ to $t^s = t^0 + s h$. For example, $s = 1$, $\beta_0 = \beta_1 = 1/2$ is the order 2 trapezoid rule: $x^1 - x^0 = \int_{t^0}^{t^1} f(t, \lambda) dt = \frac{1}{2} (f^0 + f^1)$, and $s = 2$, $\beta_0 = \beta_2 = 1/3$, $\beta_1 = 4/3$ is the order 4 Simpson’s rule: $x^2 - x^0 = \int_{t^0}^{t^2} f(t, \lambda) dt = \frac{1}{3} (f^0 + 4f^1 + f^2)$.

The coefficients $\alpha_i$ and $\beta_i$, $0 \leq i \leq s$ have the following assumptions placed on them. At least one of the coefficients $\alpha_i$ and at least one of the coefficients $\beta_i$ are nonzero so that the discretization is meaningful. At least one of $\alpha_0$ and $\beta_0$ is nonzero, and at least one of $\alpha_s$ and $\beta_s$ is nonzero, otherwise the discretization could be re-cast with a lower number of steps. Further, if all of the coefficients $\alpha_i$ and $\beta_i$ are scaled by the same factor, the discretization (2) is considered the same, so that some sort of normalization of the coefficients is also applied to remove this redundancy. Typically the normalization applied is the constraint $\alpha_s = 1$, but alternative normalizations are possible, such as $\sum_{i=0}^{s} \beta_i = 1$. One could also consider variable step size discretizations, but this paper only considers those with constant step size.
The order of the discretization $F$ is defined to be $p$ if $F$ evaluated along a solution of the ODE behaves like $h^{p+1}$ for small $h$. Precisely, the order is $p$ if

$$F(x(t^0, t^0, \xi, \lambda), x(t^1, t^0, \xi, \lambda), \ldots, x(t^s, t^0, \xi, \lambda), \lambda) = \Theta(h^{p+1}) \quad \text{as } h \to 0. \quad (3)$$

(The notation $f(z) = \Theta(g(z))$ means there exist positive constants $C_1, C_2$, and $z_0$ such that $C_1 g(z) \leq |f(z)| \leq C_2 g(z)$, for all $0 < z < z_0$ [15].) Expanding the left side of (3) as a Taylor series in $h$ around $t_0$ yields the following equivalent condition for the discretization order [16, 17]. The order is $p$ if

$$C_0 = C_1 = \cdots = C_p = 0 \quad (4)$$

but $C_{p+1} \neq 0$, where

$$C_0 = -\sum_{i=0}^{s} \alpha_i, \quad (5)$$

$$C_m = -\sum_{i=0}^{s} \frac{i^m}{m!} \alpha_i + \sum_{i=0}^{s} \frac{i^{m-1}}{(m-1)!} \beta_i, \quad m \geq 1. \quad (6)$$

$C_{p+1}$ is called the error constant, and the local discretization error for $F$ is

$$E(\xi, \lambda) := F(x(t^0, t^0, \xi, \lambda), \ldots, x(t^s, t^0, \xi, \lambda), \lambda) = C_{p+1} h^{p+1} \frac{d^{(p+1)}x(t, t^0, \xi, \lambda)}{dt^{(p+1)}} \bigg|_{t=\tau}, \quad (7)$$

for some $\tau \in [t^0, t^s]$. $E(\xi, \lambda)$ is “local” since it depends on the time interval for $F$, namely $[t^0, t^s]$. Clearly if $h$ is sufficiently small and $p$ is sufficiently large, each component of the local discretization error is close to zero. The sum of the coefficients $\alpha_i$ is zero for all discretizations that are at least order zero, since $C_0 = 0$.

2.1. Accumulated Discretizations

Accumulating a discretization in time allows one to produce a new discretization with the same order but spanning a larger time window. A compound or accumulated discretization has the form

$$F(t^0, h, \delta w + s; x^0, x^1, \ldots, x^{\delta w+s}, \lambda) = \sum_{j=0}^{w} F(t^{dj}, h, s; x^{dj}, x^{dj+1}, \ldots, x^{dj+s}, \lambda), \quad (8)$$

where $\delta$, a positive integer, is the jump size, $w$, a non-negative integer, is the accumulation index, and $t^{dj} = t^0 + \delta j h$. Thus a compound discretization is simply some base discretization added to itself but shifted forward in time by $\delta h$, this being done $w$ times. If $w = 0$, the compound discretization collapses to its base discretization.

A compound discretization is simply another discretization, albeit one with a special form. If $\hat{s}$ is the number of steps for the base discretization and its
coefficients are $\hat{\alpha}_i$ and $\hat{\beta}_i$, $0 \leq i \leq \hat{s}$, then the number of steps for the compound discretization is $s = \delta w + \hat{s}$, and its coefficients can be expressed in terms of the base coefficients as

$$\alpha_i = \sum_{j=\hat{j}}^{j_{\max}} \hat{\alpha}_{\text{mod}(i,\delta)+j}, \quad \beta_i = \sum_{j=\hat{j}}^{j_{\max}} \hat{\beta}_{\text{mod}(i,\delta)+j}, \quad 0 \leq i \leq s, \quad (9)$$

where

$$j_{\min} = \left\lceil \hat{s} - \min(\hat{s}, s-i) \mod(i,\delta) \right\rceil / \delta,$$

$$j_{\max} = \left\lfloor \min(\hat{s}, i) \mod(i,\delta) \right\rfloor / \delta,$$

and $\lfloor y \rfloor$ and $\lceil y \rceil$ are the nearest integers to $y$ satisfying $\lfloor y \rfloor \leq y$ and $y \leq \lceil y \rceil$. This allows a compound discretization to be recast in the basic form (2). The notation $F(t, h, s; x_0, \ldots, x_s, \lambda)$ is therefore sufficiently general to encompass compound discretizations also.

The obvious choices for the jump size are $\delta = 1$ or $\delta = s$, the latter being the typical way of generating compound numerical quadrature formulas [18]. For example, accumulating Simpson’s rule ($s = 2$) $w$ times with $\delta = 2$ gives the $(2w + 3)$-point compound Simpson’s rule

$$\int_{t_0}^{t_{2(w+1)}} f(t, \lambda) \, dt = h \left[ \frac{1}{3} f^0 + \frac{4}{3} f^1 + \frac{2}{3} f^2 + \frac{4}{3} f^3 + \cdots + \frac{2}{3} f^{2w} + \frac{4}{3} f^{2w+1} + \frac{1}{3} f^{2w+2} \right].$$

Accumulations with a jump size of $\delta = 1$ and an accumulation index $w \geq \hat{s}$ are of special importance. In this case the coefficients from (9) become

$$\alpha_i = \begin{cases} \sum_{j=0}^{i} \hat{\alpha}_j & \text{if } 0 \leq i < \hat{s}, \\ 0 & \text{if } \hat{s} \leq i \leq w, \\ \sum_{j=-w}^{\hat{s}-w} \hat{\alpha}_j & \text{if } w < i \leq s, \end{cases} \quad \beta_i = \begin{cases} \sum_{j=0}^{i} \hat{\beta}_j & \text{if } 0 \leq i < \hat{s}, \\ \sum_{j=-w}^{\hat{s}-w} \hat{\beta}_j & \text{if } \hat{s} \leq i \leq w, \\ \sum_{j=-w}^{\hat{s}-w} \hat{\beta}_j & \text{if } w < i \leq s, \end{cases} \quad (10)$$

where the fact that $\sum_{j=-w}^{\hat{s}-w} \hat{\alpha}_j = 0$ ($C_0 = 0$ for the base discretization) has been employed. Nothing precludes choices of $\delta$ other than 1 or $s$. For example, Köhler [19] investigates how $\delta$ affects error measures for compound Newton-Cotes formulas.

It is not difficult to show that a compound discretization has the same order as its base discretization. (See [14] for a proof of the case with $\delta = 1$; the case $\delta > 1$ is a straightforward generalization.) Further, the error constant for the compound discretization, $C_{p+1}$, is related to that of the base discretization, $\hat{C}_{p+1}$, by

$$C_{p+1} = (w+1)\hat{C}_{p+1}.$$
2.2. Symmetric Discretizations

The trapezoid rule and Simpson’s rule are examples of discretizations that have symmetric $\beta$ coefficients and anti-symmetric $\alpha$ coefficients. That is,

$$\alpha_i = -\alpha_{s-i}, \quad \text{and} \quad \beta_i = \beta_{s-i}, \quad 0 \leq i \leq \lfloor s/2 \rfloor.$$  \hfill (12)

Discretizations satisfying (12) shall be called “symmetric discretizations.” If $g(i)$ is an odd/even function about a point $s/2$, then $g(i-\delta)$ is odd/even about $(s/2)+\delta$, and their sum is odd/even about $(s+\delta)/2$. For this reason accumulations of symmetric discretizations are also symmetric.

Symmetric discretizations can have a higher order for a given number of steps, $s$, than non-symmetric ones. To see this, consider the transformation

$$\tilde{C}_0 = C_0, \quad \tilde{C}_m = \sum_{k=0}^{m} \frac{(-\frac{s}{2})^{m-k}}{(m-k)!} C_k, \quad m \geq 1.$$ \hfill (13)

From (13) it is immediately clear that system (4) is satisfied if and only if

$$\tilde{C}_0 = \tilde{C}_1 = \ldots = \tilde{C}_p = 0$$ \hfill (14)

is satisfied. Further, if (14) is satisfied, then $\tilde{C}_{p+1} = C_{p+1}$. This transformation yields

$$\tilde{C}_0 = -\sum_{i=0}^{s} \alpha_i,$$ \hfill (15)

$$\tilde{C}_m = -\sum_{i=0}^{s} \frac{(i - \frac{s}{2})^m}{m!} \alpha_i + \sum_{i=0}^{s} \frac{(i - \frac{s}{2})^{m-1}}{(m-1)!} \beta_i, \quad m \geq 1.$$ \hfill (16)

(Another way of obtaining (15)–(16) is to take the Taylor series of the left side of (3) in $h$ around the point $(t^s - t^0)/2$ rather than $t^0$.) In this form, the symmetry in the order equations is evident. The following theorem and its preceding lemma are probably not new. However, we could not find them presented in the standard texts, and so we present them here.

**Lemma 2.1.** Let $K$ be the $(s+1) \times (s+1)$ invertible matrix defined by

$$K = \begin{bmatrix} 0 & 0 & \cdots & 0 & 1 \\ 0 & \cdots & 0 & 1 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 1 & 0 & \cdots & 0 \\ 1 & 0 & \cdots & 0 & 0 \end{bmatrix}$$ \hfill (17)

If $[\alpha \beta]$ is any solution of (14), then $[-K\alpha \cr K\beta]$ is also a solution.
Proof. The equations in system (14), which are linear in $\alpha_i$ and $\beta_i$, can be divided into two groups, those with even $m$ ($C_0 = 0, C_2 = 0, \ldots$) and those with odd $m$ ($C_1 = 0, C_3 = 0, \ldots$). Defining $\alpha = [\alpha_0, \ldots, \alpha_s]^T$ and $\beta = [\beta_0, \ldots, \beta_s]^T$, the symmetry around $s/2$ in (15) and (16) allow the even group to be written in the form

$$\begin{bmatrix} P & Q \end{bmatrix} \begin{bmatrix} \alpha \\ \beta \end{bmatrix} = 0,$$

where $PK = P$ and $QK = -Q$,

and the odd group to be written in the form

$$\begin{bmatrix} R & S \end{bmatrix} \begin{bmatrix} \alpha \\ \beta \end{bmatrix} = 0,$$

where $RK = -R$ and $SK = S$,

for appropriate matrices $P, Q, R,$ and $S$. Now

$$\begin{bmatrix} P & Q \end{bmatrix} \begin{bmatrix} -K\alpha \\ K\beta \end{bmatrix} = \begin{bmatrix} -PK & QK \end{bmatrix} \begin{bmatrix} \alpha \\ \beta \end{bmatrix} = -\begin{bmatrix} P & Q \end{bmatrix} \begin{bmatrix} \alpha \\ \beta \end{bmatrix} = 0,$$

and similarly

$$\begin{bmatrix} R & S \end{bmatrix} \begin{bmatrix} -K\alpha \\ K\beta \end{bmatrix} = \begin{bmatrix} -RK & SK \end{bmatrix} \begin{bmatrix} \alpha \\ \beta \end{bmatrix} = \begin{bmatrix} R & S \end{bmatrix} \begin{bmatrix} \alpha \\ \beta \end{bmatrix} = 0.$$

Thus $\begin{bmatrix} -K\alpha \\ K\beta \end{bmatrix}$ is a solution of (14).

The following theorem illustrates the order advantage for symmetric discretizations.

**Theorem 2.2.** Any discretization of order $p$ generates a symmetric discretization of even order greater than or equal to $p$.

Proof. From the above discussion, since the transformation (13) is invertible, solutions of (4) and (14) are identical. If $\begin{bmatrix} \alpha \\ \beta \end{bmatrix}$ is any discretization, then it satisfies (4) and (14). From Lemma 2.1 and since (14) is an homogeneous linear system,

$$\begin{bmatrix} \tilde{\alpha} \\ \tilde{\beta} \end{bmatrix} = c \left( \begin{bmatrix} \alpha \\ \beta \end{bmatrix} + \begin{bmatrix} -K\alpha \\ K\beta \end{bmatrix} \right)$$

is also a solution of (14) for any constant $c$. Therefore $\begin{bmatrix} \tilde{\alpha} \\ \tilde{\beta} \end{bmatrix}$ is a discretization of order at least $p$. Further, since $K^2$ is the identity matrix, $K\tilde{\alpha} = c(K\alpha - \alpha) = -\tilde{\alpha}$ and $K\tilde{\beta} = c(K\beta + \beta) = \tilde{\beta}$ showing that this new discretization has anti-symmetric $\alpha$ coefficients and symmetric $\beta$ coefficients. The constant $c$ may be chosen to normalize this new discretization in the same manner as the original discretization. Finally, since discretizations that have anti-symmetric $\alpha$ coefficients and symmetric $\beta$ coefficients immediately satisfy $\tilde{C}_m = 0$ for all even $m$, it follows that such discretizations are of even order. In particular, if $p$ is odd, the new discretization has order at least $p + 1$. □
Remark 2.3. One could also consider discretizations that have symmetric $\alpha$ coefficients and anti-symmetric $\beta$ coefficients. However, such discretizations are not monotonic as defined in Section 2.4, so they are not considered here.

2.3. Sign-Separated Discretizations

An additional property of some discretizations that turns out to be important for accumulated versions of them is

$$\begin{cases} \alpha_i \leq 0 & \text{if } 0 \leq i \leq s/2, \\ \alpha_i \geq 0 & \text{if } s/2 \leq i \leq s \end{cases}$$

OR

$$\begin{cases} \alpha_i \geq 0 & \text{if } 0 \leq i \leq s/2, \\ \alpha_i \leq 0 & \text{if } s/2 \leq i \leq s \end{cases}. \quad (18)$$

We label such discretizations as “sign-separated” since the coefficients to the left of the mid point are the opposite sign to those on the right; we do not believe this property of discretizations has been studied before. If the discretization is normalized to make $\alpha_s = 1$, then the coefficients to the right are all nonnegative (the first case in (18)). If $s$ is even, then necessarily a sign-separated discretization has $\alpha_{s/2} = 0$. This property and the property of being symmetric are independent; for example, Euler’s method is sign-separated but not symmetric. Unlike the symmetry property, this sign-separated property need not persist when a discretization is accumulated. However, in the case where the jump size $\delta$ is 1, and the accumulation index $w$ is at least $\hat{s}$, a persistence property holds.

Theorem 2.4. If a sign-separated discretization with $\hat{s}$ steps is accumulated $w \geq \hat{s}$ times using a jump size of $\delta = 1$, then the accumulated discretization is also sign-separated.

Proof. The number of steps in the accumulated discretization is $s = w + \hat{s}$, and its $\alpha$-coefficients are given by (10). Since $w \geq \hat{s}$ it follows that $\hat{s} \leq s/2 \leq w$. Because the base discretization is sign-separated (without loss of generality assume $\hat{\alpha}_j \leq 0$ for $j \leq \hat{s}/2$), the coefficients $\alpha_i$ in (10) for $0 \leq i \leq s/2$ are either sums of only nonpositive $\hat{\alpha}_j$’s or they are sums containing all of the nonpositive $\hat{\alpha}_j$’s. In either case, since the sum of the magnitudes of the nonpositive $\hat{\alpha}_j$’s must equal the sum of the magnitudes of the nonnegative ones, it follows that $\alpha_i \leq 0$. A similar argument shows $\alpha_i \geq 0$ for $s/2 \leq i \leq s$. \qed

Remark 2.5. In Theorem 2.4, the requirement that $\delta = 1$ is essential. The requirement that $w \geq \hat{s}$ can be removed provided the base discretization is symmetric.

2.4. Monotonic Discretizations

The discretization $F$ is said to be monotonic if all the coefficients $\beta_i$, $0 \leq i \leq s$, are of the same sign or zero. Thus, of the above examples, Euler’s method, the trapezoid rule, and Simpson’s rule are monotonic, but the Adams-Bashforth order 2 method is not. Since the discretization coefficients may be normalized by any scalar, it can be assumed without loss of generality that monotonic discretizations have $\beta_i \geq 0$. From (9) it is immediately clear that if a discretization is monotonic, then any accumulated version of it is also monotonic.
Monotonic discretizations inherit the monotonicity properties of the vector field, \( f \), with respect to the parameters \( \lambda \). In particular if some component \( f_j \), \( 1 \leq j \leq m \), is nonincreasing (nondecreasing) with respect to some parameter \( \lambda_k \), \( 1 \leq k \leq q \), over some set \( \Omega \) in \( (t, x, \lambda) \)-space, then so is \( F_j \). That is, assuming smoothness of \( f \),

\[
\frac{\partial f_j}{\partial \lambda_k}(t, x, \lambda) \geq 0 \quad \forall (t, x, \lambda) \in \Omega \implies \frac{\partial F_j}{\partial \lambda_k}(t^0, h, s; x^0, \ldots, x^s, \lambda) \geq 0 \quad \forall (t^0, h, s) \text{ provided } (t^i, x^i, \lambda) \in \Omega, 0 \leq i \leq s,
\]

and a similar statement holds reversing the inequality. It is these monotonicity properties that the parameter range reduction scheme uses to exclude regions of parameter space efficiently.

The following sections define several monotonic discretizations that are analyzed in this paper. In all cases they have nonnegative \( \beta_i \) coefficients. Accumulated versions of all of these are also considered. In Section 4 it shall be seen that the relative magnitudes of the coefficients affect the efficiency of the parameter range reduction scheme. Hence we remark on this aspect as the discretizations are introduced.

2.4.1. A1OUT Discretizations

A1OUT discretizations are symmetric and only use one nonzero \( \alpha \) value at each of the outside edges, hence are necessarily sign-separated. They are defined by the following criteria:

1. \( \beta_i \geq 0 \), \( 0 \leq i \leq s \) \hspace{1cm} (monotonicity)
2. \( \alpha_i = -\alpha_{s-i} \) and \( \beta_i = \beta_{s-i} \), \( 0 \leq i \leq [s/2] \) \hspace{1cm} (symmetry)
3. \( \alpha_s = 1 \) \hspace{1cm} (normalization)
4. \( \alpha_1 = \alpha_2 = \cdots = \alpha_{s-1} = 0 \)
5. \( \beta_i \) are chosen to maximize the order, and, if this does not uniquely identify them, they are chosen to minimize the error constant, \( C_{p+1} \)

For \( 1 \leq s \leq 7 \) and \( s = 9 \), these discretizations are simply the closed Newton-Cotes formulas for numerical quadrature. For these \( s \) values the coefficients \( \beta_i \) can be determined either by solving system (4) for \( p = s + 1 \) or equivalently by interpolating a degree \( s \) polynomial through the points \( (t^i, f^i) \), \( 0 \leq i \leq s \) and then integrating this polynomial from \( t^0 \) to \( t^s \), which leads to the well known formula

\[
\beta_i = \frac{(-1)^{s-i}}{i!(s-i)!} \int_0^s \prod_{j \neq i}^{s}(t - j) \, dt, \quad 0 \leq i \leq s. \tag{19}
\]

However, for \( s = 8 \) and values of \( s \) larger than 9, (19) yields negative values for some of the \( \beta_i \), and hence the resulting discretization is not monotonic and fails to satisfy the second criterion given above for A1OUT discretizations. To obtain valid A1OUT discretizations for these values of \( s \), system (4) must be solved
Table 1: A1OUT discretizations up to $s = 17$, with order $p$ and error constant $C_{p+1}$. Half of the $\beta$ coefficients are given, the remaining are obtained by the symmetry condition $\beta_i = \beta_{s-i}$. The $\alpha$ coefficients are $\alpha_0 = -1$, $\alpha_s = 1$, and the remaining are zero.

<table>
<thead>
<tr>
<th>$s$</th>
<th>$p$</th>
<th>$C_{p+1}$</th>
<th>$\beta_0, \ldots, \beta_{\lfloor s/2 \rfloor}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>$\frac{1}{17}$</td>
<td>$\frac{1}{2}$</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>$\frac{1}{90}$</td>
<td>$\frac{1}{4}$ $\frac{3}{3}$</td>
</tr>
<tr>
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<td>4</td>
<td>$\frac{5}{80}$</td>
<td>$\frac{1}{8}$ $\frac{5}{8}$</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>$\frac{8}{95}$</td>
<td>$\frac{4}{14}$ $\frac{64}{8}$ $\frac{8}{15}$</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>275</td>
<td>90 $\frac{125}{125}$ 268 $\frac{96}{141}$</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
<td>9</td>
<td>4 $\frac{1}{140}$ $\frac{5}{35}$ $\frac{1}{140}$ $\frac{5}{35}$</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>8183</td>
<td>$\frac{525}{2509}$ $\frac{343}{20923}$</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>518400</td>
<td>17280 17280 640 17280</td>
</tr>
<tr>
<td>9</td>
<td>10</td>
<td>467</td>
<td>392240 $\frac{89600}{89600}$ $\frac{2220}{5000}$ $\frac{44800}{44800}$</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>4825</td>
<td>27535 149375 3875 16375 4345</td>
</tr>
<tr>
<td>11</td>
<td>10</td>
<td>17591827</td>
<td>61746361 $\frac{6379483}{54432000}$ 815903 $\frac{118459}{54432000}$</td>
</tr>
<tr>
<td>12</td>
<td>10</td>
<td>653184000</td>
<td>40824000 4032000 13063880 54432000</td>
</tr>
<tr>
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<td>12</td>
<td>2258256859</td>
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</tr>
<tr>
<td>14</td>
<td>12</td>
<td>2595023881</td>
<td>216835909 $\frac{55932373}{2463436800}$ 894103 $\frac{548849}{2463436800}$ $\frac{2582447}{31111757}$ 0</td>
</tr>
<tr>
<td>15</td>
<td>12</td>
<td>2586488000</td>
<td>764478000 $\frac{327498900}{488198833}$ 408375 2673000 2673000 1782000</td>
</tr>
<tr>
<td>16</td>
<td>12</td>
<td>19662645</td>
<td>20597510 $\frac{95505783}{17244057600}$ 45051392 9807885 0 $\frac{7209025}{2364795}$ 0 $\frac{630445}{399825}$</td>
</tr>
<tr>
<td>17</td>
<td>12</td>
<td>315707392</td>
<td>72855552 $\frac{6071296}{20597510}$ $\frac{3469312}{45051392}$ 3469312 236434 2207744</td>
</tr>
<tr>
<td>18</td>
<td>12</td>
<td>298438528</td>
<td>46239616 $\frac{45051392}{72855552}$ 46059264 117107392 0 $\frac{25996288}{298438528}$ 14955008 0</td>
</tr>
<tr>
<td>19</td>
<td>12</td>
<td>7023041825</td>
<td>161420925 $\frac{27785835}{46239616}$ 32837805 $\frac{138929175}{161420925}$ 12629925 12629925</td>
</tr>
<tr>
<td>20</td>
<td>12</td>
<td>35831702115</td>
<td>35662824992161 $\frac{34488115200}{7715351399}$ $\frac{15590937}{1782000}$ $\frac{9901044586361}{7715351399}$ 0 $\frac{210391762153}{15590937}$ 1059993717659 3414363256259</td>
</tr>
<tr>
<td>21</td>
<td>12</td>
<td>2855960819712000</td>
<td>126931501987200 $\frac{271996268544000}{2855960819712000}$ 0 $\frac{26444081664000}{2855960819712000}$ $\frac{1133317785600}{26444081664000}$ 96864763000 $\frac{183074115200}{183074115200}$ 3487131648000</td>
</tr>
</tbody>
</table>
with a reduced order. Table 1 gives the A1OUT discretizations for \(1 \leq s \leq 17\). The coefficients \(\beta_i\) are all relatively small in magnitude (the largest in the table is 2.67), and for each value of \(s\), the \(\beta_i\) differ from one another by at most two orders of magnitude and usually less than one.

### 2.4.2. B1OUT Discretizations

The B1OUT discretizations are analogous to the A1OUT ones with only one outer \(\beta\) value at each end (\(\beta_0\) and \(\beta_s\)) being nonzero. They are defined by the criteria:

1. \(\beta_i \geq 0, 0 \leq i \leq s\) (monotonicity)
2. \(\alpha_i = -\alpha_{s-i}\) and \(\beta_i = \beta_{s-i}, 0 \leq i \leq \lfloor s/2 \rfloor\) (symmetry)
3. \(\alpha_s = 1\) (normalization)
4. \(\beta_1 = \beta_2 = \cdots = \beta_{s-1} = 0\)
5. \(\alpha_i\) and \(\beta_i\) are chosen to maximize the order

The B1OUT discretization for \(s = 1\) is identical to the corresponding A1OUT discretization. Table 2 gives the coefficients for the B1OUT discretizations for \(s\) from 2 to 17. Although symmetric, the B1OUT discretizations are not sign-separated, unlike the A1OUT discretizations. Also the magnitudes of the \(\alpha\) coefficients tend to increase with \(s\) so that the largest at \(s = 17\) is about 1,641.

### 2.4.3. MAXORD Discretizations

MAXORD discretizations allow all coefficients \(\alpha_i\) and \(\beta_i\) to be nonzero and choose them to maximize the order. Such discretizations are useless as numerical ODE solvers since for \(s > 2\) they are unstable. However, stability is not an issue for the parameter range reduction scheme since it does not propagate errors. The MAXORD discretizations are defined by the following criteria:

1. \(\beta_i \geq 0, 0 \leq i \leq s\) (monotonicity)
2. \(\alpha_i = -\alpha_{s-i}\) and \(\beta_i = \beta_{s-i}, 0 \leq i \leq \lfloor s/2 \rfloor\) (symmetry)
3. \(\alpha_s = 1\) (normalization)
4. \(\alpha_i\) and \(\beta_i\) are chosen to maximize the order

The MAXORD discretizations for \(s = 1\) and \(s = 2\) are identical to the A1OUT discretizations. Table 3 gives the coefficients for the MAXORD discretizations from \(s = 3\) to \(s = 14\), all of which are sign-separated. The order of the \(s\)-step MAXORD discretization is \(p = 2s\). Although the order increases by two for each unit increase of \(s\), the magnitudes of both the \(\alpha\) and \(\beta\) coefficients tend to grow with \(s\). By \(s = 14\), the \(\alpha\) values get as large as \(7.42 \times 10^5\) in magnitude, and the \(\beta\) values range from about \(1.54 \times 10^{-1}\) to \(1.81 \times 10^6\).

### 2.4.4. BDF/FDF Discretizations

BDF (Backward Differentiation Formula) discretizations have only the last \(\beta_i\) coefficient nonzero and hence are necessarily monotonic but not symmetric. They are defined by the following criteria:

1. \(\beta_i \geq 0, 0 \leq i \leq s\) (monotonicity)
Table 2: B1OUT discretizations for $2 \leq s \leq 17$, with order $p$ and error constant $C_{p+1}$. The coefficients $\alpha_0$ through $\alpha_{\lfloor s/2 \rfloor}$ are given; the remaining are obtained from the symmetry condition $\alpha_{s-i} = -\alpha_i$. The coefficient $\beta_0$ is given; $\beta_s = \beta_0$ and the remaining $\beta_i$ are zero.

<table>
<thead>
<tr>
<th>$s$</th>
<th>$p$</th>
<th>$C_{p+1}$</th>
<th>$\alpha_0, \ldots, \alpha_{\lfloor s/2 \rfloor}$</th>
<th>$\beta_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>2</td>
<td>$\frac{2}{3}$</td>
<td>$-10$</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>$\frac{9}{130}$</td>
<td>$-1 \frac{27}{13}$</td>
<td>$6 \frac{6}{13}$</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>$\frac{12}{55}$</td>
<td>$-1 \frac{16}{11}$</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>$\frac{50}{1031}$</td>
<td>$-1 \frac{375}{100}$</td>
<td>$60 \frac{60}{149}$</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>$\frac{120}{959}$</td>
<td>$-1 \frac{288}{137}$</td>
<td>137</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>245</td>
<td>$-1 \frac{3430}{6894}$</td>
<td>$140 \frac{140}{383}$</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>280</td>
<td>$-1 \frac{320}{1149}$</td>
<td>140</td>
</tr>
<tr>
<td>9</td>
<td>10</td>
<td>2268</td>
<td>$-1 \frac{25515}{81499}$</td>
<td>$2520 \frac{2520}{7409}$</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>5040</td>
<td>$-1 \frac{22400}{88419}$</td>
<td>$2520 \frac{8129}{7409}$</td>
</tr>
<tr>
<td>11</td>
<td>12</td>
<td>25410</td>
<td>$-1 \frac{335412}{1121003}$</td>
<td>$27720 \frac{27720}{86231}$</td>
</tr>
<tr>
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<td>12</td>
<td>55440</td>
<td>$-1 \frac{5075670}{1088243}$</td>
<td>$27720 \frac{83711}{86231}$</td>
</tr>
<tr>
<td>13</td>
<td>14</td>
<td>22308</td>
<td>$-1 \frac{5456660}{1173173}$</td>
<td>$27720 \frac{1173173}{83711}$</td>
</tr>
<tr>
<td>14</td>
<td>14</td>
<td>48048</td>
<td>$-1 \frac{13663650}{1145993}$</td>
<td>$27720 \frac{1145993}{83711}$</td>
</tr>
<tr>
<td>15</td>
<td>16</td>
<td>375872</td>
<td>$-1 \frac{44666666}{1144993}$</td>
<td>$27720 \frac{1144993}{83711}$</td>
</tr>
<tr>
<td>16</td>
<td>16</td>
<td>720720</td>
<td>$-1 \frac{5381376}{20327869}$</td>
<td>$27720 \frac{20327869}{1195757}$</td>
</tr>
<tr>
<td>17</td>
<td>18</td>
<td>11571560</td>
<td>$-1 \frac{221306085}{81495917}$</td>
<td>$27720 \frac{81495917}{1195757}$</td>
</tr>
</tbody>
</table>
Table 3: MAXORD discretizations for $3 \leq s \leq 14$ with error constant $C_{p+1}$. Half of the coefficients are given, the remaining coefficients are obtained by the symmetry conditions $\alpha_i = -\alpha_{s-i}$ and $\beta_i = \beta_{s-i}$. The order is $p = 2s$.

<table>
<thead>
<tr>
<th>$s$</th>
<th>$C_{p+1}$</th>
<th>$\alpha_0, \ldots, \alpha_{[s/2]}$</th>
<th>$\beta_0, \ldots, \beta_{[s/2]}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>15 56</td>
<td>-1 -27/11</td>
<td>3 -27/11</td>
</tr>
<tr>
<td>4</td>
<td>1 2625</td>
<td>-1 32/5</td>
<td>6 96/25</td>
</tr>
<tr>
<td>5</td>
<td>5 63294</td>
<td>-1 -1625 -2000/137 137</td>
<td>30 750/3 0000/137 137</td>
</tr>
<tr>
<td>6</td>
<td>1 294294</td>
<td>-1 -132 -375/0 7</td>
<td>10 360 2250/49 49</td>
</tr>
<tr>
<td>7</td>
<td>1 186873</td>
<td>-1 -9947 -16121 -42875/363</td>
<td>70 3430 10290/85750 363</td>
</tr>
<tr>
<td>8</td>
<td>1 166499</td>
<td>-1 -28544 -208544 -395136/0</td>
<td>140 8960 109760 439040 686000</td>
</tr>
<tr>
<td>9</td>
<td>1 329281</td>
<td>-1 -350649 -359184 -109653024 -8001504/7129 7129</td>
<td>1260 102060 1632960 8899560 20003760</td>
</tr>
<tr>
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</tr>
<tr>
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<td>13800 1677060 41926500 37738500 1509354000 95833840</td>
</tr>
<tr>
<td>12</td>
<td>1 415382</td>
<td>-1 -620208 -12272732 -102753200 -331518825/6617 6617 6617 6617 6617</td>
<td>13800 1906580 60574600 670824000 3396046500 1183335360</td>
</tr>
<tr>
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<td>-1 -128087297 -332225052 -32294942108/1145993 1145993 1145993 1145993 1145993</td>
<td>180180 30450420 1096215120 14738003280 92112520500 6394566120</td>
</tr>
<tr>
<td>14</td>
<td>1 7573179</td>
<td>-1 -153984068 -4784206973 -56653037168/1171733 1171733 1171733 1171733 1171733 1171733</td>
<td>180180 35315280 1492070580 23873129280 18054054080 212227472320</td>
</tr>
</tbody>
</table>
2. \( \alpha_s = 1 \) (normalization)
3. \( \beta_0 = \beta_1 = \cdots = \beta_{s-1} = 0 \)
4. \( \alpha_i \) are chosen to maximize the order

BDF discretizations with \( s \leq 7 \) are used for the numerical solution of stiff ODEs due to their large stability regions; for larger values of \( s \) they become unstable. Table 4 gives the coefficients for these discretizations for \( 1 \leq s \leq 14 \). The order of these discretizations is \( p = s \). These discretizations are not sign-separated.

The FDF (Forward Differentiation Formula) discretizations are the symmetric counterpart to BDF discretizations. Specifically, if \( \alpha \) and \( \beta \) are the BDF coefficient vectors, then the coefficient vectors for the FDF discretization are \(-K\alpha\) and \(K\beta\), where \( K \) is defined by (17). FDF discretizations have the same order as the BDF ones, are also monotonic but not symmetric, and have the normalization \( \alpha_0 = -1 \) rather than \( \alpha_s = 1 \). BDF discretizations and accumulated versions of them were used by Willms [14] and are included here to allow comparison of the effectiveness of the parameter range reduction scheme with various discretizations.

3. The Parameter Range Reduction Scheme

For system (1) with initial condition \((t^0, \xi)\), if the model parameters are known precisely, \( \lambda = \lambda^* \), and if the recorded time series data for the variables are without noise, \( x^\text{obs}_n = x(t^n, t^0, \xi, \lambda^*) \), then the discretization \( F(2) \) evaluates to \( E \), the local discretization error. (If the time step size is sufficiently small, then \( E \) is near zero.) However, in a real situation the recorded data are noisy so that the observed values of the model variables are not points but ranges of values. In addition, for the parameter identification problem, the parameters are not known values but ranges. For these reasons, \( F \) also evaluates to a range. If the variable ranges and the parameter ranges encompass their “true” values, this range for \( F \) includes \( E \). The main idea of the parameter range reduction scheme is to select subranges for the parameters, evaluate the resulting range for \( F \), and discard that subrange as inconsistent with the data if the range for \( F \) does not include \( E \).

The input to the parameter range reduction scheme is an ordinary differential equation model, an initial range for each parameter in the model, and, for each \( t \) in some interval \( I \), a range for each model variable; that is, the ranges for the variables are time dependent. The scheme’s assumption is that each parameter and variable lies within its range. As mentioned above, the initial ranges for the parameters may be as large as \((-\infty, \infty)\) if no information about the parameter is known, or they can incorporate any known constraints or information, for example if the parameter is necessarily positive, or between zero and one, etc. For the variable ranges, as a prerequisite for the scheme, the recorded discrete time series data set must be transformed to ranges continuous in time. Szusz and Willms [20] give an effective algorithm for replacing discrete data with a continuous piecewise linear band that encloses all the data and is minimal in height subject to a certain smoothness constraint. This algorithm is employed
Table 4: BDF discretizations for $1 \leq s \leq 14$, with error constant $C_{p+1}$. The coefficients $\beta_0, \ldots, \beta_{s-1}$ are all zero. The order is $p = s$. The FDF coefficients can be obtained from these using $\alpha_i \mapsto -\alpha_{s-i}$ and $\beta_i \mapsto \beta_{s-i}$.

<table>
<thead>
<tr>
<th>$s$</th>
<th>$C_{p+1}$</th>
<th>$\alpha_0, \ldots, \alpha_s$</th>
<th>$\beta_s$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$1$</td>
<td>$1$</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>$\frac{3}{2}$</td>
<td>$\frac{1}{3}, -\frac{1}{3}$</td>
<td>$\frac{2}{3}$</td>
</tr>
<tr>
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<td>$\frac{11}{12}$</td>
<td>$-2, 9, -18$</td>
<td>$6$</td>
</tr>
<tr>
<td>4</td>
<td>$\frac{10}{125}$</td>
<td>$3, -16, 36, -48$</td>
<td>$12$</td>
</tr>
<tr>
<td>5</td>
<td>$\frac{147}{157}$</td>
<td>$-12, 75, -200, 300, -300$</td>
<td>$25$</td>
</tr>
<tr>
<td>6</td>
<td>$\frac{20}{343}$</td>
<td>$-10, -24, 75, -900, 150, -120$</td>
<td>$137$</td>
</tr>
<tr>
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<td>$\frac{35}{372}$</td>
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</tr>
<tr>
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<td>$\frac{280}{6849}$</td>
<td>$-35, -320, 3920, -3136, 4900, -15680, 3920, -2240$</td>
<td>$280$</td>
</tr>
<tr>
<td>9</td>
<td>$\frac{252}{7129}$</td>
<td>$-252, -280, 2835, -12960, 35280, -63504, 73810, -73810, 1$</td>
<td>$140$</td>
</tr>
<tr>
<td>10</td>
<td>$\frac{2520}{8191}$</td>
<td>$-2520, -2800, 2835, -12960, 35280, -63504, 73810, -73810, 1$</td>
<td>$2520$</td>
</tr>
<tr>
<td>11</td>
<td>$\frac{2310}{1118273}$</td>
<td>$-2520, -2800, 2835, -12960, 35280, -63504, 73810, -73810, 1$</td>
<td>$27720$</td>
</tr>
<tr>
<td>12</td>
<td>$\frac{27720}{83711}$</td>
<td>$-27720, -2800, 2835, -12960, 35280, -63504, 73810, -73810, 1$</td>
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</tr>
<tr>
<td>13</td>
<td>$\frac{25740}{1145993}$</td>
<td>$-25740, -2800, 2835, -12960, 35280, -63504, 73810, -73810, 1$</td>
<td>$1145993$</td>
</tr>
<tr>
<td>14</td>
<td>$\frac{24024}{1171733}$</td>
<td>$-24024, -2800, 2835, -12960, 35280, -63504, 73810, -73810, 1$</td>
<td>$1171733$</td>
</tr>
</tbody>
</table>
to generate the initial ranges for the model variables, but other methods could also be used. It should be emphasized again that whatever means is used to generate continuous ranges for the data, the results will be somewhat arbitrary depending ultimately on what the user thinks is a fair representation for the data. The consistency checks described below are based on these constructed data ranges and so are dependent on them.

3.1. Notation

The following notations for ranges will simplify the exposition. Briefly speaking, a bold type face denotes a range or Cartesian product of ranges (a box), and under and over bars denote lower and upper values of ranges. The magnitude of a range is its length. The reader is reminded that superscripts and subscripts are used as time and spatial indices, respectively, and that \( x^i \) is an approximation to the solution of the ODE at time \( t^i \), that is, to \( x(t^i, t^0, \xi, \lambda) \).

Thus

\[
\lambda := \lambda_1 \times \lambda_2 \times \cdots \times \lambda_q,
\]

\[
\lambda_j := \left[ \lambda_j, \bar{\lambda}_j \right], \quad 1 \leq j \leq q,
\]

\[
|\lambda_j| := \bar{\lambda}_j - \lambda_j, \quad 1 \leq j \leq q,
\]

\[
x(t) := x_1(t) \times x_2(t) \times \cdots \times x_m(t), \quad t \in I,
\]

\[
x_j(t) := \left[ x_j(t), \bar{x}_j(t) \right], \quad 1 \leq j \leq m, \quad t \in I.
\]

For given values of \( t^0, h, \) and \( s \), define

\[
x^i := x(t^i), \quad \text{provided} \quad t^i = t^0 + ih \in I, \quad 1 \leq i \leq s,
\]

and as a further notational simplification define

\[
X := x^0, x^1, \ldots, x^s \quad \text{and} \quad \bar{X} := \bar{x}^0, \bar{x}^1, \ldots, \bar{x}^s.
\]

The range of the \( j \)th component of the discretization \( F \) over \((X, \lambda)\) is defined to be

\[
F_j(X, \lambda) := \left[ (\bar{F}_j, F_j) \right] := \left[ \min_{\lambda \in \lambda} F_j(X, \lambda), \max_{\lambda \in \lambda} F_j(X, \lambda) \right], \quad 1 \leq j \leq m. \quad (20)
\]

3.2. The Inconsistency Test and Monotonicity

The question to be answered is: What points in \( \lambda \) yield model solutions that lie within the variable ranges \( x(t) \) for all time in the interval \( I \) in the range reduction scheme attacks this question by eliminating subregions of \( \lambda \) that admit no model solutions that lie within \( x(t) \) for \( t \) in some subinterval \([t^0, t^s] \subseteq I \). The scheme uses two facts:
1. For any discretization $F$ over $[t^0, t^s] \subseteq I$, if $F_j(X, \lambda)$ does not enclose the discretization error $E_j(\xi, \lambda)$, $1 \leq j \leq m$, for some $(\xi, \lambda) \in (x^0, \lambda)$, then all parameter values $\lambda$ in $\lambda$ are inconsistent with the data. That is, no solution, $x(t, t^0, \xi, \lambda)$, of the model stays within the variable ranges $x(t)$, $t \in [t^0, t^s]$.

2. If the $j$th component, $f_j(t, x, \lambda)$, of the vector field is either monotonic nondecreasing or monotonic nonincreasing with respect to each of the parameters $\lambda_k$, $1 \leq k \leq q$, for all $(t^i, x^i) \in (t^i, x^i)$, $0 \leq i \leq s$, and all $\lambda \in \lambda$, then for a monotonic discretization $F$,

$$F_j(X, \lambda) = \left[ \min_{X \in X} F_j(X, \lambda_{\text{min}}), \max_{X \in X} F_j(X, \lambda_{\text{max}}) \right],$$

(21)

where $\lambda_{\text{min}}$ and $\lambda_{\text{max}}$ are the critical values of $\lambda$ whose $k$th components, $1 \leq k \leq q$, are given by

$$\lambda_{\text{min}}^k = \begin{cases} \lambda_k & \text{if } f_j \text{ is monotonic nondecreasing with } \lambda_k, \\ \lambda_k & \text{if } f_j \text{ is monotonic nonincreasing with } \lambda_k, \end{cases}$$

$$\lambda_{\text{max}}^k = \begin{cases} \lambda_k & \text{if } f_j \text{ is monotonic nondecreasing with } \lambda_k, \\ \lambda_k & \text{if } f_j \text{ is monotonic nonincreasing with } \lambda_k. \end{cases}$$

This greatly simplifies the computation of $F_j$ since for each of its two end points only a single point in parameter space need be considered, not the whole region $\lambda$. Monotonicity with respect to the variables $x_j$, $1 \leq j \leq m$, leads to further simplifications for computing $F_j$. However, the situation is different since the variables are involved explicitly in $F$ and are also independent at each time step. If $-\alpha_i x_j^i + h \beta_i f_j(t^i, x^i, \lambda)$ is monotonic with respect to $x_k^i$ for all $(t^i, x^i) \in (t^i, x^i)$ and all $\lambda \in \lambda$, then the minimization and maximization of $F_j$ in (21) over this component of $X$ is replaced with computation at one of the end points of $x_k^i$.

The first fact provides a test for consistency of portions of parameter space that involves two quantities, $F_j$ and $E_j$. The second fact provides a simple method for computing $F_j$. Unfortunately, computing $E_j$ or even an estimate of it is non-trivial, since it depends on the solution of the model itself for a given $\lambda$ and initial point $\xi$. If one wished to expend the effort to compute a numerical approximation to such a solution, it would be possible to determine directly if it stayed within $x$. This is the essential idea in the parameter identification approach used in [8, 9, 11, 12, 21, 22, 23, 24]. Instead, this scheme simply assumes $E_j = 0$. This approximation is made more acceptable by ensuring that the step size $h$ is chosen sufficiently small and the order $p$ is sufficiently large. Nonetheless, there is the possibility that by approximating $E_j$ as zero, the scheme could declare inconsistent a region of parameter space that has some points that are in fact consistent. However, in most situations the noise in the data, that is the width of the ranges $x_j(t)$, will account for variations in $F$ of much larger size than $|E|$. Therefore, except in very low noise situations, it is
likely that setting $E_j = 0$ will not significantly affect the results of the scheme. Evidence for this claim is provided in Section 4.

### 3.3. Exploitation of Monotonicity

It turns out that many models exhibit monotonicity with respect to the parameters and variables, and it is for this reason that monotonic discretizations are used in the parameter range reduction scheme, permitting the exploitation of these properties of the vector field. Further, even though a vector field may not be monotonic with respect to a parameter over all valid values of the variables, it is often the case that over a restricted discretization time window, which also restricts the variable ranges, the vector field does exhibit monotonicity with respect to the parameter, and this is all that is needed to calculate $F$ efficiently as described above.

For example, consider the model

$$
\begin{align*}
x'_1 &= f_1(t, x, \lambda) = \lambda_1 x_1 - x_2^2, \\
x'_2 &= f_2(t, x, \lambda) = \lambda_3 \sin(t) x_2,
\end{align*}
$$

(22)

(here $\lambda_2$ is a power, not a superscript on $x_2$) and the 2-step monotonic discretization

$$
F = -(x^2 - x^0) + h \left[ \frac{1}{2} f(t^0, x^0, \lambda) + f(t^1, x^1, \lambda) + \frac{1}{2} f(t^2, x^2, \lambda) \right].
$$

(23)

Suppose for illustrative purposes that $h$ has been chosen, and that the initial ranges for the parameters satisfy the following conditions:

$$
-2/h \leq \lambda_1, \quad \lambda_1 \leq 0, \quad 0 \leq \lambda_2, \quad -2/h \leq \lambda_3, \quad \lambda_3 \leq 0.
$$

(24)

Further, suppose that data have been recorded for this system for $0 \leq t \leq 6$, and that these recordings have been translated into bands for the variables as shown in Figure 1. The first component of $F$ is

$$
F_1 = -(x_1^2 - x_1^0) + h \left[ \frac{1}{2} (\lambda_1 x_0^1 - (x_2^0)^{\lambda_2}) + (\lambda_1 x_1^1 - (x_2^1)^{\lambda_2}) + \frac{1}{2} (\lambda_1 x_2^1 - (x_2^2)^{\lambda_2}) \right].
$$

Differentiating $F_1$ with respect to $\lambda_1$ gives

$$
\frac{\partial F_1}{\partial \lambda_1} = h \left[ \frac{1}{2} x_1^0 + x_1^1 + \frac{1}{2} x_1^2 \right].
$$

If $x_i^1 \geq 0$, $0 \leq i \leq 2$, then $F_1$ is monotonic nondecreasing with respect to $\lambda_1$, and is monotonic nonincreasing if $x_1^1 \leq 0$. In relation to Figure 1, if the discretization window is chosen so that $[t^0, t^2] \subseteq [0, T_1]$ or $[t^0, t^2] \subseteq [T_2, 6]$, then $F_1$ is monotonic nonincreasing with respect to $\lambda_1$. Similar arguments show that if $[t^0, t^2] \subseteq [0, T_3]$ or $[t^0, t^2] \subseteq [T_6, 6]$, then $F_1$ is monotonic nonincreasing with respect to $\lambda_2$, and if $[t^0, t^2] \subseteq [T_4, T_5]$, then $F_1$ is monotonic nondecreasing with respect to $\lambda_2$. Finally, if $[t^0, t^2] \subseteq [0, \pi]$ ($[\pi, 6]$), then $F_2$ is monotonic.
Figure 1: Bands for the variables for system (22) over the time interval [0, 6]. The solid and dashed lines are for \( x_1 \) and \( x_2 \), respectively. The labelled time points are where monotonicity of the vector field with respect to the parameters may be altered, that is, when \( x_1 \) crosses 0, when \( x_2 \) crosses 1, and when \( t \) crosses \( \pi \). The shaded time intervals are those over which the model is monotonic with respect to all of the parameters.

The model is monotonic with respect to all of the parameters if the discretization window, \([t^0, t^2]\), lies within one of the intervals \([0, T_3]\), \([T_4, \pi]\), \([\pi, T_1]\), or \([T_6, 6]\). Determining whether a specific discretization time window yields a model that is monotonic with respect to the parameters over that window is simply a function of the parameter ranges and the ranges of the variables over that window. The parameter range reduction scheme only selects discretization windows that yield monotonicity with respect to all of the parameters.

Like many models, the vector field for this model also has monotonicity properties with respect to the variables. Given the parameter range restrictions (24), \( F_1 \) is monotonic nondecreasing with respect to \( x_1^0 \) and is monotonic nonincreasing with respect to \( x_1^1 \), \( x_2^1 \), \( x_0^1 \), \( x_0^2 \), \( x_1^2 \), and \( x_2^2 \) over the entire data window. The component \( F_2 \) is monotonic nondecreasing with respect to \( x_0^2 \) and is monotonic nonincreasing with respect to \( x_2^2 \) over the entire data window. If \([t^0, t^2] \subseteq [0, \pi]\), then \( F_2 \) is monotonic nonincreasing with respect to \( x_2^1 \), and this property is reversed if \([t^0, t^2] \subseteq [\pi, 6]\).

For example, if the discretization window is chosen such that \([t^0, t^2] \subseteq [0, T_3]\),
the ranges of $F_1$ and $F_2$ are given by:

$$F_1 = -\left(x_1^2 - x_0^2\right) + h \left[\frac{1}{2} \left(\lambda_1 x_0^2 - \lambda_1 x_2^2\right) + \left(\lambda_1 x_1^2 - \lambda_1 x_2^2\right)\right]$$

$$F_1 = -\left(x_1^2 - x_0^2\right) + h \left[\frac{1}{2} \left(\lambda_1 x_0^2 - \lambda_1 x_2^2\right) + \left(\lambda_1 x_1^2 - \lambda_1 x_2^2\right)\right]$$

$$F_2 = -\left(x_2^2 - x_0^2\right) + h \left[\frac{1}{2} \left(\lambda_3 \sin(t) x_0^2 - \lambda_3 \sin(t) x_2^2\right) + \left(\lambda_3 \sin(t) x_1^2 - \lambda_3 \sin(t) x_2^2\right)\right]$$

$$F_2 = -\left(x_2^2 - x_0^2\right) + h \left[\frac{1}{2} \left(\lambda_3 \sin(t) x_0^2 - \lambda_3 \sin(t) x_2^2\right) + \left(\lambda_3 \sin(t) x_1^2 - \lambda_3 \sin(t) x_2^2\right)\right]$$

In this case, the ranges $F_1$ and $F_2$ are determined with just four computations and without optimizing over the variable ranges $X$. The scheme permits a lack of monotonicity with respect to the variables since maximizing or minimizing $F_j$ with respect to a variable can be done simply by considering the function $ax^j + f(t^i, x^i, \lambda)$, where $a = -\alpha_i / (h \beta_i)$. For example, if the first condition on $\lambda_1$ in (24) was replaced by $\lambda_1 \leq -2/h$, then $F_1$ no longer would be monotonic with respect to $x_1^0$ over the whole range $\lambda_1$, but its other monotonicity properties remain. The lower bound on $F_1$ is then

$$\underline{F_1} = \min_{x_0^0 \in \mathbb{x}_0^0} \left\{ -\left(x_1^2 - x_1^0\right) + h \left[\frac{1}{2} \left(\lambda_1 x_0^2 - \lambda_1 x_2^2\right) + \left(\lambda_1 x_1^2 - \lambda_1 x_2^2\right)\right] \right\}$$

and a similar expression exists for $\underline{F_1}$. Even though $F_1$ is not monotonic with respect to $x_1^0$, the function being minimized on the right side of (29) is: its derivative with respect to $x_1^0$ is

$$1 + \frac{h}{2} \lambda_1,$$

which is nonnegative if $\lambda_1 \geq -2/h$, and nonpositive if $\lambda_1 \leq -2/h$. In the former case, (25) is unaltered, while in the latter $x_0^0$ should be replaced with $\overline{x}_0^0$ in (25).

3.4. General Outline

The general outline of the parameter range reduction scheme to reduce a single box in parameter space is given below.
Parameter Range Reduction Using Monotonicity

1. while progress on reducing the box is being made do
2. for each model equation \( j = 1, \ldots, m \), do
3. select discretizations \( F \), i.e., values \( t_0, h, \) and \( s \), so that \( f_j(t, x, \lambda) \)
   is monotonic with respect to each of the parameters \( \lambda_k, 1 \leq k \leq q, \)
   for all \((t^i, x) \in (t^i, x^i), 0 \leq i \leq s, \) and all \( \lambda \in \lambda \)
4. for each selected discretization do
5. compute \( F_j(X, \lambda^{\text{min}}) \)
6. if \( F_j > 0 \) then the parameter box is inconsistent; return; end if
7. for each parameter \( \lambda_k, 1 \leq k \leq q, \) do
8. move the value of \( \lambda_k^{\text{min}} \) toward \( \lambda_k^{\text{max}} \) until \( F_j(X, \lambda^{\text{min}}) > 0 \)
   or \( \lambda_k^{\text{min}} = \lambda_k^{\text{max}}, \)
9. if \( f_j \) is monotonic nondecreasing with \( \lambda_k \) then
10. update \( X_k \) to the new value of \( \lambda_k^{\text{min}} \)
11. else (\( f_j \) is monotonic nonincreasing with \( \lambda_k \))
12. update \( X_k \) to the new value of \( \lambda_k^{\text{min}} \)
13. end if
14. end do (for each parameter)
15. repeat steps 5 to 14 with all lower bars replaced by upper bars,
   superscripts “min” replaced by “max”, and the inequalities in
   steps 6 and 8 reversed
16. end do (for each discretization)
17. end do (for each equation)
18. end do (while progress)

Most of the work involved in the selection of discretizations in step 3 is completed
in the first iteration of the while loop. Since the size of the parameter box is being maintained or reduced each iteration, each time window over
which \( f_j(t, x, \lambda) \) is monotonic with respect to each of the parameters \( \lambda_k \) for all \((t^i, x) \in (t^i, x^i)\) and all \( \lambda \in \lambda \) is either remaining the same size or growing.
In subsequent iterations then, the discretizations can be selected as the same
as the previous iteration, or some work can be expended to see if the time
windows of monotonicity can be extended. Since \( t_0 \) and \( h \) are real variables,
the number of possible discretizations that could be selected is infinite. The
scheme attempts to select a reasonable number of discretizations that produce
“independent” reductions. Here there is a trade-off between selecting enough
discretizations to sample the information available in the time trace adequately
and keeping the number of discretizations and hence computation time small.
Step 8 is performed by first moving \( \lambda_k^{\text{min}} \) all the way to \( \lambda_k^{\text{max}} \)
and testing if \( F_j > 0 \). If so, then \( \lambda_k^{\text{min}} \) is moved back to where \( F_j \approx 0 \)
by an iterative secant method. The outer while loop is present because reductions in \( \lambda \) achieved
by some discretizations and for some of the model equations in general will allow
new reductions to be achieved by other discretizations that may have already
been processed in the current iteration.

To maintain simple box-shaped regions in parameter space, the scheme reduces the initial box by only cutting off “slices” from one of the faces. That is,
for a fixed $k$, $1 \leq k \leq q$, one of $\lambda_k$ or $\overline{\lambda}_k$ is moved toward the other, and the resulting region is removed if it fails the consistency test. Limiting the geometry of the parameter space in this way means that the final reduced box obtained by the scheme may still be fairly large. Further reductions could be possible if more complicated regions were removed from the box, for example choosing two indices $k_1$ and $k_2$ and altering both $\lambda_{k_1}$ and $\lambda_{k_2}$. However, the price paid for these further reductions is a remaining region that is considerably more complicated to specify or work with than a box. The other alternative is to split the box into two or more boxes whenever reduction ceases. The disadvantage of this last approach is a potential combinatorial explosion in the number of boxes. The scheme has been implemented so that it splits boxes in half when reduction ceases; the split being in the parameter with the current largest range. A cap on the total number of boxes produced has been imposed.

4. Analytic Results

In this section the parameter range reduction scheme is applied analytically to two simple models, and the results for various discretizations are compared. In addition, analysis of the suitability of assuming the discretization error, $E$, is zero is made.

Consider the prototypical equation

$$x' = \lambda x.$$  \hfill (30)

Before applying the range reduction scheme to reduce the range for $\lambda$, the term $-\theta E$ is added to the discretization (2), where $E$ is the discretization error given by (7), and $\theta$ is an analysis parameter. Setting $\theta$ equal to zero corresponds to ignoring the discretization error as done by the range reduction scheme, while setting $\theta$ equal to one corresponds to the ideal case of having complete knowledge of the discretization error value and using this knowledge in the range reduction scheme. In this way the effect of the approximation $E = 0$ can be ascertained. Thus the value of interest is

$$G = F_1 - \theta E = -\sum_{i=0}^{s} \alpha_i x^i + h \sum_{i=0}^{s} \beta_i \lambda x^i - \theta E.$$  \hfill (31)

Suppose $\lambda^*$ is the “true” value of the parameter and that $x^{*i}$ is the “true” value of $x$ at time $t^i$ using an initial condition of $x^{*0} = 1$. The data can be scaled by any factor, and this results in the same scaling of $G$, which does not affect the locations of its zeros. Hence using this initial condition is completely general. Suppose the ranges for the variable $x$ are given by $x^i = [x^{*i} - \epsilon_x, x^{*i} + \epsilon_x]$, $0 \leq i \leq s$, where $\epsilon_x$ is the noise magnitude. This restriction of having the true solution lying exactly in the middle of the range is done to simplify the analysis; however, the more general case yields similar results. Using the fact that the discretization error is given by

$$E = -\sum_{i=0}^{s} \alpha_i x^{*i} + h \sum_{i=0}^{s} \beta_i \lambda^* x^{*i},$$
the upper value of the range $G$ becomes

$$G = \sum_{i=0}^{s} (\lambda h \beta_i - \alpha_i) \left( x^{s_i} - \sigma^i(\lambda) \epsilon x \right) - \theta E$$

$$= \sum_{i=0}^{s} (\alpha_i - \lambda h \beta_i) \sigma^i(\lambda) \epsilon x + h(\lambda - \lambda^*) \sum_{i=0}^{s} \beta_i x^{s_i} + (1 - \theta) E,$$

where

$$\sigma^i(\lambda) = \text{sign} \left( \alpha_i - \lambda h \beta_i \right) = \begin{cases} 1 & \text{if } \alpha_i - \lambda h \beta_i > 0, \\ 0 & \text{if } \alpha_i - \lambda h \beta_i = 0, \\ -1 & \text{otherwise}, \end{cases} \quad 1 \leq i \leq s. \quad (32)$$

To determine $\lambda$, the algorithm effectively solves $G = 0$ for $\lambda$ yielding

$$\lambda = \frac{\lambda^* h \sum_{i=0}^{s} \beta_i x^{s_i} - \epsilon x \sum_{i=0}^{s} \alpha_i \sigma^i(\lambda) + (\theta - 1) E}{h \sum_{i=0}^{s} \beta_i \left( x^{s_i} - \epsilon x \sigma^i(\lambda) \right)}$$

$$= \frac{\lambda^* - A(\lambda) \frac{\epsilon x}{M} + \frac{(\theta - 1) E}{M h \sum_{i=0}^{s} \beta_i}}{1 - B(\lambda) \frac{\epsilon x}{M}}, \quad (33)$$

where $L = h s$ is the window length,

$$M = \frac{\sum_{i=0}^{s} \beta_i x^{s_i}}{\sum_{i=0}^{s} \beta_i}, \quad A(\lambda) = \frac{s \sum_{i=0}^{s} \alpha_i \sigma^i(\lambda)}{\sum_{i=0}^{s} \beta_i}, \quad \text{and} \quad B(\lambda) = \frac{\sum_{i=0}^{s} \beta_i \sigma^i(\lambda)}{\sum_{i=0}^{s} \beta_i}. \quad (34)$$

Similarly, solving $\mathcal{G} = 0$ for $\lambda$ yields

$$\bar{\lambda} = \frac{\lambda^* + A(\bar{\lambda}) \frac{\epsilon x}{M} + \frac{(\theta - 1) E}{M h \sum_{i=0}^{s} \beta_i}}{1 + B(\bar{\lambda}) \frac{\epsilon x}{M}}, \quad (35)$$

The quantity $M$ is a weighted average of the true $x$ values over the discretization window. Hence, the factor $\epsilon x / M$ should be viewed as a relative noise magnitude. Since the discretization error $E$ is linear in the coefficients $\alpha$ and $\beta$, its magnitude is dependent on the normalization applied to the discretization; the factor $E / \left( \sum_{i=0}^{s} \beta_i \right)$ is a normalized discretization error, and dividing this quantity by $M$ gives a relative normalized error value. Although it appears that expressions (33) and (35) are implicit since they involve $\lambda$ and $\bar{\lambda}$ on the right hand side in the arguments of $A$ and $B$, in reality they are explicit. The set of points $\{\alpha_i / (h \beta_i)\}_{i=0}^{s}$ partitions the $\lambda$ axis into a set of regions on each of which the $\sigma^i$ (and hence $A$ and $B$) are constant so that (33) and (35) give a well-defined curves for $\lambda$ and $\bar{\lambda}$ respectively. Moreover, since $G$ is continuous across these partition boundaries, these curves also are continuous. Order the partition points $p_i = \alpha_i / h \beta_i$, $0 \leq i \leq s$, with the permutation $\mu$ so that $p_{\mu(0)} \leq p_{\mu(1)} \leq \cdots \leq p_{\mu(s)}$. Since the $\beta_i$ are nonnegative, each $p_i$ has the same
Theorem 4.1. For any discretization of order at least one and with \( \alpha \) and only if discretizations considered in this paper have larger values of \( \sum_k \) one so that \( \tilde{\alpha} \) nonnegative

\[
A(\lambda) = \begin{cases} 
0 & \text{if } \lambda < p_{\mu(0)}, \\
\sum_{i=0}^{s} \left( \sum_{j=0}^{m} -\alpha_{\mu(j)} + \sum_{j=m+1}^{s} \alpha_{\mu(j)} \right) & \text{if } p_{\mu(m)} < \lambda < p_{\mu(m+1)}, \\
0 & \text{if } p_{\mu(s)} < \lambda.
\end{cases}
\]

As \( \lambda \) increases from \(-\infty\) it passes through the points \( p_{\mu(j)} \), so that \( m \) increases in the above expressions. It is not difficult to see that the term inside the parentheses in the above expression for \( A \) is always nonnegative, so \( A \geq 0 \), and the maximum value for \( A \) occurs when \( m = k \) and is given by

\[
A_0 = \frac{s \sum_{i=0}^{s} |\alpha_i|}{s \sum_{i=0}^{s} \beta_i}.
\]

Further, in the limit as \( h \to 0 \), \( A \to A_0 \). The following theorem shows that A1OUT discretizations have the smallest possible value of \( A_0 \), but all other discretizations considered in this paper have larger values of \( A_0 \).

**Theorem 4.1.** For any discretization of order at least one and with \( \sum_{i=0}^{s} \beta_i > 0 \), the minimum value for \( A_0 \) is 2. Furthermore, the minimum is achieved if and only if \( \alpha_s = -\alpha_0 > 0 \) and \( \alpha_i = 0 \) for \( 1 \leq i \leq s - 1 \).

**Proof.** By hypothesis \( \sum_{i=0}^{s} \beta_i \) is positive, and the discretization is at least order one so that \( C_1 = 0 \) (16), that is, \( \sum_{i=0}^{s} \beta_i = \sum_{i=0}^{s} (i - \frac{s}{2}) \alpha_i \). Therefore,

\[
\sum_{i=0}^{s} \beta_i = \left| \sum_{i=0}^{s} \left( i - \frac{s}{2} \right) \alpha_i \right| \leq \sum_{i=0}^{s} \left| \left( i - \frac{s}{2} \right) \alpha_i \right| \leq \frac{s}{2} \sum_{i=0}^{s} |\alpha_i|.
\]

Consequently,

\[
A_0 = \frac{s \sum_{i=0}^{s} |\alpha_i|}{s \sum_{i=0}^{s} \beta_i} \geq \frac{s}{2} \sum_{i=0}^{s} |\alpha_i| = 2.
\]

The first inequality in (37) is a strict equality if and only if \( \alpha_s \) has the same sign as \((i - s/2)\) for \( 0 \leq i \leq s \), and the second inequality is a strict equality if and only if \( \alpha_i = 0 \) for \( 1 \leq i \leq s - 1 \). In addition, since the discretization is at least order one, it satisfies \( C_0 = \sum_{i=0}^{s} \alpha_i = 0 \) (5). Together these imply that \( A_0 \) achieves its minimum value if and only if \( \alpha_s = -\alpha_0 > 0 \) and \( \alpha_i = 0 \) for \( 1 \leq i \leq s - 1 \). \( \square \)

The expression for \( B \) may be given as

\[
B(\lambda) = \begin{cases} 
1 & \text{if } \lambda < p_{\mu(0)}, \\
\frac{1}{\sum_{i=0}^{s} \beta_i} \left( \sum_{j=0}^{m} -\beta_{\mu(j)} + \sum_{j=m+1}^{s} \beta_{\mu(j)} \right) & \text{if } p_{\mu(m)} < \lambda < p_{\mu(m+1)}, \\
-1 & \text{if } p_{\mu(s)} < \lambda.
\end{cases}
\]
Clearly \(|B| \leq 1\), and in the limit as \(h \to 0\), \(B \to B_0\), where

\[
B_0 = \frac{\sum_{i=0}^{s} c_i \beta_i}{\sum_{i=0}^{s} \beta_i}, \quad c_i = \begin{cases} 
\text{sign}(\alpha_i) & \text{if } \alpha_i \neq 0, \\
\text{sign}(\lambda) & \text{otherwise}.
\end{cases}
\] (38)

If the discretization is symmetric and all \(\alpha_i\) are nonzero, which is the case for MAXORD when \(s\) is odd, and for B1OUT, then \(B_0 = 0\), but this is not generally the case otherwise. Further, if the discretization is symmetric, it is not difficult to show that \(|B| \geq |B_0|\). It should be noted that both the quantities \(A\) and \(B\) are dependent on the discretization but are independent of the normalization applied to the discretization and are independent of the data.

From (33) and (35) the magnitude of \(\lambda\) is computed as

\[
|\lambda| = \frac{2 \varepsilon_x}{M} \left( \frac{A}{L} - B \left( \lambda^* + \frac{(\theta - 1)E}{Mh \sum_{i=0}^{s} \beta_i} \right) \right).
\] (39)

The form of this equation along with those of (33) and (35) provide insight into the range obtained for \(\lambda\) detailed below.

First, as expected, the bounds on \(\lambda\) get worse as the noise magnitude, \(\varepsilon_x\), becomes larger, and get better better as \(\varepsilon_x\) decreases. If the discretization error, \(E\), is known and used (\(\theta = 1\)), then both \(\lambda\) and \(\lambda^\ast\) tend toward \(\lambda^*\) as the noise magnitude, \(\varepsilon_x\), tends to zero. From (39), the magnitude of \(\lambda\) is smaller if \(A/L\) is small, \(B\) is small, and/or the relative noise is small. If \(A = 0\) then assuming the normalized relative error is not too large, \(|\lambda|\) is proportional to \(\lambda^*\).

Second, the effect of ignoring the discretization error \(E\) (\(\theta = 0\)) is a translation of the true parameter value \(\lambda^*\) and it is only significant if the error is relatively large compared to the noise as seen by the numerators of (33) and (35).

Taking a Taylor series of \(\lambda\) in the variables \(\varepsilon_x\) and \(E\) gives

\[
\lambda = \lambda^* + \left( \lambda^* B - \frac{A}{L} \right) \frac{\varepsilon_x}{M} - \left( \frac{E}{Mh \sum_{i=0}^{s} \beta_i} \right) + \cdots.
\]

As a coarse approximation, if \(|E/Mh \sum_{i=0}^{s} \beta_i|\) is small compared to either \(|A\varepsilon_x/ML|\) or \(|\lambda^* Be_x/M|\) then ignoring \(E\) has little effect on \(\lambda\). On the other hand, if \(|E/Mh \sum_{i=0}^{s} \beta_i|\) is relatively large, then ignoring it may result in either \(\lambda < \lambda^*\), or \(\lambda^\ast < \lambda^*\) so that the range no longer includes the true value of the parameter. This can be seen in Fig. 2, left plot, where \(\lambda\) has been generated from a low order, \((s = 1, \text{ order } 2)\) A1OUT discretization using a large step size, \(h = 1.9\). In this plot, \(\lambda\) lies below \(\lambda^*\) when the relative noise, \(\varepsilon_x/M\) is below about 0.2. This undesirable effect can be mitigated by reducing \(h\) and/or increasing the order. Even for the relatively large step size used in the right plot of Fig. 2, \(h = 0.95\), the discretization with \(s = 2\) (order 4) is sufficiently accurate so that ignoring the discretization error \(E\) has very little effect on \(\lambda\). In both plots of Fig. 2, the extreme right edges of the curves represent the maximum noise possible while keeping the band around \(x^\ast\) completely positive, that is, \(\varepsilon_x \leq \min_{t_0 \leq t \leq t^\ast} |x^\ast(t)|\). The reason that the curves do not extend as far in the
Figure 2: Bounds for $\lambda$ given by (33) and (35) for the A1OUT discretization on a window of length $L = hs = 1.9$ with $\lambda^* = 1$ and $w = 0$. Left plot: $s = 1$, $h = 1.9$; right plot: $s = 2$, $h = 0.95$. The solid curves give the relative bounds on $\lambda$ for the case where the discretization $E$ is ignored, $\theta = 0$, while the dashed curves are the bounds in the ideal case where the discretization error is known and used, $\theta = 1$. The two curves are almost indistinguishable in the right plot.

The left plot is because the weighted average $M$ of the rising exponential $x$ for the A1OUT discretization is larger for the $s = 1$ case. For the remaining analysis, it is assumed that the reduction algorithm ignores the discretization error, that is $\theta = 0$.

Third, if the window length $L = hs$ is too small compared to the noise, $\epsilon_x$, then very little range reduction for $\lambda$ is possible. In the limit as $h \to 0$, we have

$$
\lambda_\Delta = \frac{\lambda^* - A_0 \frac{\epsilon_x}{ML}}{1 - B_0 \frac{\epsilon_x}{M}} \quad \text{and} \quad \lambda_\Theta = \frac{\lambda^* + A_0 \frac{\epsilon_x}{ML}}{1 + B_0 \frac{\epsilon_x}{M}}. \quad (40)
$$

If $h$ approaches zero and $s$ is held fixed (so that $A_0$ and $B_0$ are fixed but $L$ decreases), then the bounds on $\lambda$ will get worse for all discretizations due to the $A_0/L$ term in the numerators of (40). This is shown in Figure 3. In other words, as the discretization window becomes shorter, the noise magnitude becomes more important; the signal-to-noise ratio is decreasing. This can be understood by observing that the set of possible slopes of a line connecting a point on the left edge of the data window to one on the right is much larger when the window is tall and thin (large noise, small $L$) than when it is short and fat (small noise, large $L$). The reason for the differences between the discretizations in Figure 3 is the value of $A_0$, as discussed in the next paragraph.

Fourth, assuming $h$ is small enough to make $E$ insignificant, the value of $A_0$ is the primary determinant on the bounds for $\lambda$. Discretizations that have small values of $A_0$ yield smaller ranges for $\lambda$ than those that have large values of $A_0$. Comparatively, $B_0$ has a minor influence on $\lambda$. Table 5 gives values for $A_0$ for the different unaccumulated discretizations considered in this study. The minimal value of $A_0$ is obtained by the A1OUT discretization for all values of $s$ when $w = 0$ because $C_1 = 0$ reduces to the equation $s = \sum_{i=0}^{s} \beta_i$ for this discretization. The value of $A_0$ for the MAXORD discretization tends to
Figure 3: Bounds for $\lambda$ given by (33) and (35) for the five unaccumulated discretizations for $s = 7$ as a function of the step size $h$, with $\lambda^* = 1$. The noise level is $\epsilon_x = 0.2$. Other values of $s$ and $\epsilon_x$ gave similar results.

Table 5: $A_0$ values for different unaccumulated discretizations with step values from 1 to 14.

<table>
<thead>
<tr>
<th>$s$</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
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<tr>
<td>A1OUT</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>MAXORD</td>
<td>2</td>
<td>2</td>
<td>3.8</td>
<td>3.524</td>
<td>4.976</td>
<td>4.673</td>
<td>5.918</td>
</tr>
<tr>
<td>BDF/FDF</td>
<td>2</td>
<td>8</td>
<td>20</td>
<td>42.67</td>
<td>85.33</td>
<td>166.4</td>
<td>322.1</td>
</tr>
<tr>
<td>B1OUT</td>
<td>2</td>
<td>2</td>
<td>20</td>
<td>18</td>
<td>85.33</td>
<td>65</td>
<td>322.1</td>
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</table>

<table>
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<tr>
<th>$s$</th>
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<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
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<tbody>
<tr>
<td>A1OUT</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>8</td>
<td>2</td>
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<td>2</td>
</tr>
<tr>
<td>BDF/FDF</td>
<td>624.2</td>
<td>1214.</td>
<td>2373.</td>
<td>4658.</td>
<td>9178.</td>
<td>18135.</td>
<td>35914.</td>
</tr>
<tr>
<td>B1OUT</td>
<td>210</td>
<td>1214.</td>
<td>689.5</td>
<td>4658.</td>
<td>2356.</td>
<td>18135.</td>
<td>8337.</td>
</tr>
</tbody>
</table>
rise with $s$ but dips a little for each even $s$, since $\alpha_{s/2} = 0$ when $s$ is even for this symmetric discretization. The BDF and FDF discretizations have rapidly increasing values of $A_0$ as $s$ increases. The B1OUT discretization has the same values for $A_0$ as BDF/FDF when $s$ is odd; when $s$ is even, so that by symmetry $\alpha_{s/2}$ is zero, the value of $A_0$ is better for B1OUT than for BDF/FDF, but it is still much worse than A1OUT and is increasing for each even $s$. The values of $B_0$ for the five discretizations are given in Table 6. The values of $B_0$ for BDF/FDF are the worst possible at $\pm 1$; indeed, for these two discretizations, $B$ itself is always $\pm 1$. For A1OUT the value of $|B_0|$ increases rapidly toward 1 as $s$ increases. The MAXORD discretization has $B_0 = 0$ for odd $s$ and slowly decreasing values of $|B_0|$ for even increasing $s$. The B1OUT discretization has the best value of $B_0$. Fig. 4 shows the bounds obtained by these unaccumulated discretizations as a function of the noise for various values of $s$ and a fixed $h$. Clearly the A1OUT and MAXORD discretizations perform much better than the BDF and B1OUT discretizations. (The FDF discretization performed even worse than BDF; not shown.) For A1OUT and MAXORD the bounds get better as $s$ increases, but they get worse for BDF/FDF and B1OUT. As $s$ increases, $L$ also increases. For A1OUT, which has $A_0 = 2$ for all $s$, the improvement in the bounds is because the data window is larger. For MAXORD, the increase in $L$ outweighs the increase in $A_0$ as $s$ increases. However, for BDF/FDF and B1OUT the rapid increase in $A_0$ with $s$ causes a far greater detrimental effect than the beneficial effect of increasing $L$. Fig. 5 shows the bounds obtained by various unaccumulated discretizations as a function of $h$ using $\lambda^* = 1$, a fixed data window $L = 1$ and a relative error of $\epsilon_x = 0.2$ (other values of $\lambda^*$, $L$ and $\epsilon_x$ give qualitatively similar results). As $h$ decreases in this figure $s$ and hence the order increase for all the discretizations. Thus the figure shows that despite a decreasing step size and an increasing order, the bounds on $\lambda$ are getting worse for all the discretizations except A1OUT. The reason for this is the increase of

Table 6: $B_0$ values for different unaccumulated discretizations with step values from 1 to 14. The value is positive if $\lambda > 0$ and negative if $\lambda < 0$.

<table>
<thead>
<tr>
<th>s</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1OUT</td>
<td>0</td>
<td>±.6667</td>
<td>±.7500</td>
<td>±.8444</td>
<td>±.8681</td>
<td>±.9024</td>
<td>±.9131</td>
</tr>
<tr>
<td>MAXORD</td>
<td>0</td>
<td>±.6667</td>
<td>0</td>
<td>±.5143</td>
<td>0</td>
<td>±.4329</td>
<td>0</td>
</tr>
<tr>
<td>BDF</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>FDF</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
</tr>
<tr>
<td>B1OUT</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>s</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1OUT</td>
<td>±.9257</td>
<td>±.9362</td>
<td>±.9422</td>
<td>±.9477</td>
<td>±.9529</td>
<td>±.9565</td>
<td>±.9595</td>
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<tr>
<td>MAXORD</td>
<td>±.3807</td>
<td>0</td>
<td>±.3437</td>
<td>0</td>
<td>±.3157</td>
<td>0</td>
<td>±.2936</td>
</tr>
<tr>
<td>BDF</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
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</tr>
<tr>
<td>FDF</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
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<td>-1</td>
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<tr>
<td>B1OUT</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Figure 4: Bounds for $\lambda$ given by (33) and (35) for four unaccumulated discretizations with a step size of $h = 0.1$, $\lambda^* = 1$, and a window of length $L = hs$. $s = 2$ solid curves; $s = 5$, dashed curves; $s = 8$ dot-dot-dash curves; $s = 13$ dotted curves. The vertical scales differ on these plots.

Figure 5: Bounds on $\lambda$ given by (33) and (35) as a function of the step size $h$ for different unaccumulated discretizations. $\lambda^* = 1$, $L = 1$, $\epsilon_x = 0.2$. 

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$A_0$ with $s$. (Actually, the bounds for $\lambda$ generated by A1OUT also get slightly worse as $h$ decreases because $M$, the weighted average of $x$, decreases mildly with increasing $s$ for this model.) The symmetric discretization B1OUT and the non-symmetric discretizations BDF and FDF display very poor behaviour as $h$ decreases. Due to the scale, the figure does not show the bounds for these three discretizations for $h$ below about 0.25. However, as $h$ continues to decrease, the bounds get worse by several orders of magnitude. Although the value of $A_0$ is the primary determinant, the value of $B_0$ has a small effect. The reason that FDF does worse than BDF is that for the former, $B_0 = -1$ while for the latter, $B_0 = 1$. Hence, the factor in the denominator of (33) and (35) makes matters worse for FDF when $\lambda^* > 0$. BDF does worse than FDF when $\lambda^* < 0$.

The following conclusions can be drawn from the above observations. If $h$ is chosen too large, then the discretization error, $E$, may adversely affect $\lambda$, that is, cause it to exclude the true parameter value. The step size $h$ must be sufficiently small. If the data window $L = hs$ is too small, then the bounds on $\lambda$ will be poor. The window length $L$ must be sufficiently large. Discretizations that have $A_0$ values that increase rapidly with $s$ yield very poor bounds for $\lambda$ when $s$ is large. It would appear that using an A1OUT discretization with a large value of $s$ is the best solution. Unfortunately, computing the A1OUT coefficients for large $s$ (hence high order) becomes very difficult, and of course, the coefficients must be stored to higher precision to achieve the given order.

Appropriate accumulation of a discretization will allow one to use a very large value of $s$ without the need to compute correspondingly high order coefficients. What is more, if the base discretization is sign-separated, then these accumulations of it have $A_0$ values that approach 2 as $s$ increases. Consider a base discretization $F(t^\alpha, h, \hat{s}; X, \lambda)$ with coefficients $\hat{\alpha}_i$ and $\hat{\beta}_i$, $0 \leq i \leq \hat{s}$. Accumulate this discretization $w$ times with $w \geq \hat{s}$ and a jump size of $\delta = 1$. Then the accumulated discretization has $s = \hat{s} + w$ steps, and its coefficients are given in terms of the base case discretization’s coefficients by (10) and (11).

Suppose the length of the data window, $L = sh = (\hat{s} + w)h = \hat{s}h$, is fixed. Previously it was argued that as $h \to 0$, $A \to A_0$, and that, for at least some discretizations, $A_0$ may grow as $s$ increases (Table 5). However, it turns out that for accumulated discretizations with $\delta = 1$ and $w \geq \hat{s}$, the factor $A_0$ often decreases with increasing $w$. Two results in this direction are presented below.

**Theorem 4.2.** If the partial $\alpha$ sums

$$S_i = \sum_{j=0}^{i} \hat{\alpha}_j, \quad 0 \leq i \leq \hat{s} - 1,$$

of a base discretization of at least order zero are alternating in sign,

$$\text{sign}(S_i) = (-1)^i \text{sign}(S_0), \quad 0 \leq i \leq \hat{s} - 1,$$  \hspace{1cm} (41)

then any accumulation of the base discretization with jump size $\delta = 1$ and
accumulation index \( w \geq \hat{s} \) has

\[
A_0 = \frac{(\hat{s} + w)\hat{A}_0}{(w + 1)\hat{s}}.
\]

**Proof.** The coefficients of the accumulated discretization in terms of the base discretization are given by (10) and (11). Thus

\[
A_0 = \frac{s}{\sum_{i=0}^{\hat{s}} \beta_i} \left( \frac{(\sum_{i=0}^{\hat{s}-1} \alpha_j) + \sum_{i=1}^{\hat{s}} |\sum_{j=1}^{\hat{s}} \alpha_j|}{(w + 1) \sum_{j=0}^{\hat{s}} \beta_j} \right).
\]

Since \( \hat{C}_0 = 0 \), we have

\[
\text{sign} \left( \sum_{j=i}^{\hat{s}} \alpha_j \right) = \text{sign} \left( -\sum_{j=0}^{i-1} \alpha_j \right) = -\text{sign}(S_{i-1}).
\]

Using the alternating partial sum property (41), \( A_0 \) becomes

\[
A_0 = \frac{(\hat{s} + w)\text{sign}(S_0)}{(w + 1) \sum_{j=0}^{\hat{s}} \beta_j} \left( \sum_{j=0}^{\hat{s}-1} (-1)^j \sum_{i=0}^{j} \hat{\alpha}_j + \sum_{j=1}^{\hat{s}} (-1)^j \sum_{i=1}^{j} \hat{\alpha}_j \right).
\]

Since \( \hat{C}_0 = 0 \), expanding the left \( i \) sum to include the term \( i = \hat{s} \) and expanding the right \( i \) sum to include the term \( i = 0 \) simply adds zero twice. Therefore,

\[
A_0 = \frac{(\hat{s} + w)\text{sign}(S_0)}{(w + 1) \sum_{j=0}^{\hat{s}} \beta_j} \sum_{j=0}^{\hat{s}} (-1)^j \left( \sum_{i=0}^{j} \hat{\alpha}_j \right) = \frac{(\hat{s} + w)\text{sign}(S_0)}{(w + 1) \sum_{j=0}^{\hat{s}} \beta_j} \sum_{i=0}^{\hat{s}} (-1)^i \hat{\alpha}_i.
\]

In order for (41) to hold, it is necessary that the \( \hat{\alpha}_j \) also alternate in sign, and since \( \text{sign}(S_0) = \text{sign}(\hat{\alpha}_0) \), we have

\[
\text{sign}(S_0) \sum_{i=0}^{\hat{s}} (-1)^i \hat{\alpha}_i = \sum_{i=0}^{\hat{s}} |\hat{\alpha}_i|.
\]

Therefore,

\[
A_0 = \frac{(\hat{s} + w)\sum_{i=0}^{\hat{s}} |\hat{\alpha}_i|}{(w + 1) \sum_{j=0}^{\hat{s}} \beta_j} = \frac{(\hat{s} + w)\hat{A}_0}{(w + 1)\hat{s}}.
\]

Thus appropriate accumulated versions of discretizations that satisfy the alternating sign property (41) have \( A_0 \) values bounded above by \( 2\hat{A}_0/\hat{s} \) (since \( w \geq \hat{s} \)) and, as \( w \) increases, \( A_0 \to \hat{A}_0/\hat{s} \). It can be verified easily that the BDF (and FDF) discretizations given in Table 4 satisfy this property. Hence, accumulated BDF/FDF discretizations should perform significantly better than unaccumulated versions. The B1OUT discretizations do not have alternating partial sums, but they almost do, and the \( A_0 \) values for accumulated versions of this discretization end up being a little above what this theorem dictates.

A stronger result for \( A_0 \) holds when the base discretization is sign-separated.
Theorem 4.3. If a base discretization of at least order one is sign-separated, then any accumulation of it with jump size $\delta = 1$ and accumulation index $w \geq \hat{s}$ has

$$A_0 = \frac{2(\hat{s} + w)}{w + 1}.$$  

Proof. Starting from (42), separate each of the sums on $i$ into two and use the fact that the sum of the $\hat{\alpha}_j$ is zero. Hence, $\sum_{j=0}^{q-1} \hat{\alpha}_j = -\sum_{j=q+1}^{\hat{s}} \hat{\alpha}_j$, giving

$$A_0 = \frac{(\hat{s} + w)}{(w + 1) \sum_{j=0}^{\hat{s}} \beta_j} \left( \sum_{i=0}^{\lceil \frac{\hat{s}}{2} \rceil - 1} \sum_{j=0}^{i} \hat{\alpha}_j + \sum_{i=\lceil \frac{\hat{s}}{2} \rceil}^{\hat{s}-1} \sum_{j=i+1}^{\hat{s}} \hat{\alpha}_j + \sum_{j=1}^{\hat{s}} \sum_{i=\lceil \frac{\hat{s}}{2} \rceil + 1}^{\hat{s}} \hat{\alpha}_j \right),$$

where $\lceil y \rceil$ is the smallest integer greater than or equal to $y$. Re-assigning the summation index $i$ on the second and third sums to match the fourth and first, respectively, and collecting gives

$$A_0 = \frac{2(\hat{s} + w)}{(w + 1) \sum_{j=0}^{\hat{s}} \beta_j} \left( \sum_{i=0}^{\lceil \frac{\hat{s}}{2} \rceil - 1} \sum_{j=0}^{i} \hat{\alpha}_j + \sum_{i=\lceil \frac{\hat{s}}{2} \rceil}^{\hat{s}} \sum_{j=i+1}^{\hat{s}} \hat{\alpha}_j \right).$$

Since the base discretization is sign-separated, the terms inside the first absolute value are all nonpositive, and the terms inside the second one are all nonnegative. Hence,

$$A_0 = \frac{2(\hat{s} + w)}{(w + 1) \sum_{j=0}^{\hat{s}} \beta_j} \left( - \sum_{i=0}^{\lceil \frac{\hat{s}}{2} \rceil - 1} \sum_{j=0}^{i} \hat{\alpha}_j + \sum_{i=\lceil \frac{\hat{s}}{2} \rceil}^{\hat{s}} \sum_{j=i+1}^{\hat{s}} \hat{\alpha}_j \right) = \frac{2(\hat{s} + w)}{(w + 1) \sum_{j=0}^{\hat{s}} \beta_j} \sum_{j=0}^{\lceil \frac{\hat{s}}{2} \rceil} \left( \sum_{i=0}^{\lceil \frac{\hat{s}}{2} \rceil - 1} \hat{\alpha}_j + \sum_{i=\lceil \frac{\hat{s}}{2} \rceil}^{\hat{s}} \left( j - \lceil \frac{\hat{s}}{2} \rceil \right) \hat{\alpha}_j \right),$$

(43)

The two sums in (43) now may be combined, and adding the term with $j = \lceil \frac{\hat{s}}{2} \rceil$ simply adds zero, so

$$A_0 = \frac{2(\hat{s} + w)}{(w + 1) \sum_{j=0}^{\hat{s}} \beta_j} \sum_{j=0}^{\hat{s}} \left( j - \lceil \frac{\hat{s}}{2} \rceil \right) \hat{\alpha}_j.$$  

If $\hat{s}$ is even, we have $\lceil \frac{\hat{s}}{2} \rceil = \frac{\hat{s}}{2}$; but if $\hat{s}$ is odd, $\lceil \frac{\hat{s}}{2} \rceil = \frac{\hat{s} + 1}{2}$. In the latter case,

$$\sum_{j=0}^{\frac{\hat{s}}{2}} \left( j - \frac{\hat{s}}{2} \right) \hat{\alpha}_j = \sum_{j=0}^{\frac{\hat{s}}{2}} \left( j - \frac{\hat{s}}{2} \right) \hat{\alpha}_j - \sum_{j=0}^{\frac{\hat{s}}{2}} \frac{1}{2} \hat{\alpha}_j = \sum_{j=0}^{\frac{\hat{s}}{2}} \left( j - \frac{\hat{s}}{2} \right) \hat{\alpha}_j,$$
Figure 6: Bounds for \( \lambda \) given by (33) and (35) for four discretizations and some accumulations with jump size \( \delta = 1 \). The true parameter value is \( \lambda^* = 1 \), the base discretization has \( \hat{s} = 12 \), the window length is \( L = 1 \), and the step size is given by \( h = L/(\hat{s} + w) \). \( w = 0 \), solid curves; \( w = 12 \), dashed curves; \( w = 24 \), dot-dash curves; \( w = 120 \), dotted curves. The vertical scales differ on these plots.

since \( \sum_{j=0}^{\hat{s}} \hat{\alpha}_j = 0 \). Therefore, in both cases,

\[
A_0 = \frac{2(\hat{s} + w)}{(w + 1) \sum_{j=0}^{\hat{s}} \hat{\beta}_j} \sum_{j=0}^{\hat{s}} \left( j - \frac{\hat{s}}{2} \right) \hat{\alpha}_j.
\]

Finally, the base discretization satisfies \( \hat{C}_1 = 0 \). Hence, by (16), we have the stated result. \( \square \)

Thus accumulating with \( \delta = 1 \) has the advantage of reducing \( A_0 \) for sign-separated discretizations such as MAXORD, which otherwise have increasing values for \( A_0 \) with \( s \). For the A1OUT discretization, accumulating in this manner actually causes an increase in \( A_0 \), but \( A_0 < 4 \) and \( A_0 \to 2 \) as \( w \to \infty \). Fig. 6 shows the effect of accumulating on the various discretizations over a fixed window of length \( L = 1 \). Accumulating has very little effect on the bounds for A1OUT (they get slightly worse when \( w > 0 \) except the upper bound at high noise levels). In comparison, the MAXORD bounds and the BDF bounds im-
prove as \( w \) increases, since their \( A_0 \) values are decreasing as dictated by Theorem 4.3 and Theorem 4.2, respectively. The B1OUT bounds also improve with increasing \( w \) since, as mentioned above, the B1OUT discretizations almost satisfy property (41). However, in all cases the improvement saturates for large \( w \), and the A1OUT and MAXORD bounds are vastly superior to those given by BDF and B1OUT.

From a geometric point of view, accumulating a sign-separated discretization with \( \delta = 1 \) results in a new discretization that “looks” more and more like A1OUT as \( w \) increases — the variable \( x \) is only used very near the two ends of the discretization window with negative coefficients on the left end and positive ones on the right, and the vector field \( f \) is evaluated at all points in the discretization.

As mentioned above, a compound discretization has the same order as its base discretization, and its error constant is \((w+1)\) times the base discretization error constant. Since \( w \approx L/h \) as \( h \) gets small, the term \( sE/L \) behaves like \( (w+1)sE/L \), and hence also approaches zero as \( h \) decreases provided the order \( p \) is at least two. The term \( B \) remains bounded by one independent of \( w \).

As a mild generalization of the above analysis, consider a system of ODEs where the first equation is of the form

\[
x' = \lambda x y + z, \tag{44}
\]

where \( x \) here stands for the first variable, and \( y \) and \( z \) are functions of the remaining variables and parameters. In this case, the bounds for \( \lambda \) become

\[
\lambda = \frac{\lambda^* - \xi \sigma + A(\lambda) \xi^\sigma + (\theta - 1) sE \xi \sum_{i=0}^s \beta_i}{1 + B(\lambda) \xi^\sigma + H(\lambda) \xi^\sigma + J(\lambda) \xi^\sigma} \tag{45}
\]

\[
\bar{\lambda} = \frac{\lambda^* + \xi \sigma - A(\lambda) \xi^\sigma + (\theta - 1) sE \xi \sum_{i=0}^s \beta_i}{1 - B(\lambda) \xi^\sigma - H(\lambda) \xi^\sigma + J(\lambda) \xi^\sigma}. \tag{46}
\]

where

\[
\sigma(\lambda) = \text{sign}(\lambda h \beta_i y \sigma^i - \alpha_i), \quad \rho(\lambda) = \text{sign}(\lambda x \sigma^i),
\]

\[
M = \frac{\sum_{i=0}^s \beta_i x \sigma^i y \sigma^i}{\sum_{i=0}^s \beta_i}, \quad A(\lambda) = \frac{s \sum_{i=0}^s \alpha_i \sigma^i(\lambda)}{\sum_{i=0}^s \beta_i},
\]

\[
B(\lambda) = \frac{\sum_{i=0}^s \beta_i y \sigma^i \sigma^i(\lambda)}{\sum_{i=0}^s \beta_i} , \quad H(\lambda) = \frac{\sum_{i=0}^s \beta_i x \sigma^i \rho^i(\lambda)}{\sum_{i=0}^s \beta_i},
\]

\[
J(\lambda) = \frac{\sum_{i=0}^s \beta_i \sigma^i(\lambda) \rho^i(\lambda)}{\sum_{i=0}^s \beta_i}.
\]

The main difference to \( \lambda \) for this more complicated model is the fact that uncertainties in \( y \) and \( z \) cause \(|\lambda|\) to increase. The coefficients multiplying the noise factors are a bit different from the simpler case: \( M \) is now the weighted average of \( x \sigma^i y \sigma^i \) over the time window, rather than just \( x \sigma^i \); \( B \) is not bounded by one but by the maximum magnitude of \( y \sigma^i \) over the window; the corresponding
quantity $H$ is bounded by the maximum magnitude of $x^*$; $J$ is bounded by one; the important quantity $A$ is bounded by $\sum_{i=0}^* |\alpha_i| / \sum_{i=0}^* |\beta_i|$ as before. The conclusions are essentially the same as the simpler model: 1) $h$ must be chosen small enough so that the discretization error $E$ is insignificant compared to the noise magnitude, 2) discretizations that have a smaller value for $A_0$ are likely to perform better, 3) decreasing $h$ while holding $s$ constant results in a larger range for $\lambda$ due to increased dominance of the data noise, 4) accumulation of a discretization allows $h$ to decrease without shrinking the time window and hence avoiding noise dominance.

5. Empirical Results

The preceding section describes how different discretizations affect the estimation ability of the range reduction algorithm when applied to simple models. This section provides empirical evidence that the results from the previous section also apply to more complex models. The first model considered is of a nonlinear pendulum and is two-dimensional with three unknown parameters. The data were simulated by numerically integrating the model with high precision using a selected “true” parameter set, sampling at a high frequency, and then adding noise. The second model is a four-dimensional model of drug absorption and metabolism involving seven parameters and is fit to experimental pharmacokinetic data. In contrast to the large, dense data set of the first model, this data set is very small and relatively sparse.

For both models, the range reduction algorithm was applied with a limit of 10,000 parameter boxes. At that point, the total volume of the consistent boxes was determined as a fraction of the original volume of parameter space. This number raised to the power $1/q$, where $q$ is the number of parameters, was used as a measure, $\mu$, of how well the algorithm performed. That is,

$$
\mu = \left( \frac{\text{volume of consistent boxes}}{\text{volume of original box}} \right)^{1/q} = \left( \sum_{i=1}^n \prod_{j=1}^q |\lambda_{ij}| / |\lambda_{0j}| \right)^{1/q}, \tag{47}
$$

where $n$ is the number of consistent boxes, and $\lambda_{ij}$ is the range for the $j$th parameter of box $i$, box 0 being the original parameter box. The measure $\mu$ takes on values between 0 and 1, where a smaller number indicates that more progress was made in reducing the parameter ranges. If there was just one consistent box and all parameter ranges were reduced to roughly half their original ranges, then $\mu$ would be approximately 0.5. Various step sizes $h$, step numbers $s$, and accumulation indices $w$ were used for each discretization.

5.1. Nonlinear, Forced Pendulum

A nonlinear pendulum of length $L$, mass $m$, and damping coefficient $a$ that is exposed to a sinusoidal force of size $b$ at frequency $\omega$ is governed by

\begin{align*}
x' & = y, \\
y' & = -\frac{g}{L} \sin(x) - \frac{a}{m} y + \frac{b}{mL} \sin(\omega t), \tag{48}
\end{align*}
where $g$ is the gravitational constant. Suppose the parameters of the forcing function, $b$ and $\omega$, are precisely known, as is $g$, and the task is to determine the intrinsic parameters $L$, $m$, and $a$ from time series data. As discussed in [14], defining new parameters $A = 1/L$, $B = a/m$, and $C = 1/mL$ alters the second equation to

$$y' = -gA \sin(x) - By + Cb \sin(\omega t),$$

which has better monotonic properties for $A$, $B$, and $C$ than the original equation had for $L$, $m$, and $a$. The penalty for such a transformation is that the boxes in the new parameter space are necessarily inflated to enclose all the original parameter values.

The true parameters were chosen as

$$L = 0.5, \quad m = 0.6, \quad a = 0.05, \quad b = 1.4, \quad \omega = 2, \quad g = 9.8,$$

and the system was integrated for 100 seconds starting at an initial condition of $[x, y] = [3, 0]$ and sampled at an interval of 0.1 seconds (1001 points). Normally distributed noise with a standard deviation equal to one percent of the maximum amplitude of each variable over the time interval was added to the sampled data. The resulting time series is shown in Fig. 7. Continuous bands for these data were generated by the TASLE program described in [20] using $t_{\text{min}} = 0.2$ for

Figure 7: Simulated data for the nonlinear pendulum and continuous bands generated by the TASLE program [20] using $t_{\text{min}} = 0.2$ for both $x$ and $y$. The heights of the bands are 0.249 for $x$ and 0.798 for $y$ and can be seen in the inset magnifications of the indicated portion of the time series.
Table 7: Original parameter ranges, the transformed ranges enclosing them, the hull of the consistent parameter boxes obtained by A1OUT with \( s = 12 \) and \( h = 0.05 \), and the ranges of the original parameters enclosing this best hull.

Original parameter ranges:

\[
L = [0.005, 50] \quad m = [0.006, 60] \quad a = [0.005, 5] \n\]

Transformed parameter ranges enclosing the above:

\[
A = [0.2, 200] \quad B = [8.33 \times 10^{-6}, 833] \quad C = [3.33 \times 10^{-4}, 3.33 \times 10^4] \n\]

Best hull of consistent boxes:

\[
A = [1.60, 2.35] \quad B = [8.33 \times 10^{-6}, 0.687] \quad C = [1.27, 5.86] \n\]

Best hull in terms of original parameters:

\[
L = [0.426, 0.623] \quad m = [0.274, 1.84] \quad a = [0.005, 1.26] \n\]

Figure 8: Best values of \( \log_{10} \mu \) for the five unaccumulated discretizations over values of \( h \) ranging from 0.001 to 0.2.

Both \( x \) and \( y \). The heights of the resulting bands are 0.249 for \( x \) and 0.798 for \( y \). Each of the original parameters was given an initial range from 0.01 to 100 times the true value, see Table 7. The best measure (\( \mu = 4.654 \times 10^{-4} \)) was achieved by A1OUT with \( s = 7 \) and \( h = 0.05 \). The hull of consistent boxes for this reduction was computed, and the resulting ranges for \( A, B, \) and \( C \) were converted back to the original parameters, displayed in Table 7. For all parameters, substantial reductions in the ranges were achieved with the most reduction occurring for the parameter \( L \) and the least for \( a \). This is not surprising since the range reduction algorithm employs local consistency tests over relatively short time windows, while the affect of the parameter \( a \) on the system is a slow decay in amplitude of the oscillations over a long time period.

In comparison to the other discretizations, A1OUT performed the best followed by MAXORD and then, much poorer, BDF, FDF, and B1OUT. Values of \( \log_{10}(\mu) \) for these discretizations for \( 1 \leq s \leq 14 \) and \( 0.001 \leq h \leq 0.2 \) are shown in Figure 8. The pattern displayed in this figure is what is expected given the
values of $A_0$ for these discretizations as a function of $s$ (Table 5). The only two surprises are that B1OUT performed poorer than FDF/BDF for almost all values of $s$ rather than performing better for even $s$, and FDF performed better than all other discretizations at $s = 1$. The value of $h$ for this reduction was $0.2$, and it is possible that the first order FDF method for this large step size performed anomalously well due to fortuitous influence of the discretization error $E$.

Figure 9 shows that as $h$ is decreased while holding $s$ constant, in this case $s = 4$, all of the discretizations perform worse since the noise in the data dominates the variation of $F$ when the window length gets too small. Other values of $s$ give similar results.

The effect of accumulating a discretization on the performance of the range reduction algorithm is not as clear for the nonlinear pendulum model as it was for the simple model of the previous section. For all of the discretizations, accumulation first brought improvements in performance, but then as $w$ was increased further, the performance got worse, Figure 10. As given in Theorems 4.2 and 4.3, once $s = \hat{s} + w$ is about ten times as large as $\hat{s}$, the value of $A_0$ is within about 10% of its limiting value, so that very little further improvement in $A_0$ can be made. Therefore, it is not surprising that Figure 10 shows improvements in performance for all of the discretizations continued until $s$ was between five times and ten times the value of $\hat{s} = 6$. The reason for the poorer performance as $w$ is increased further is not clear.

5.2. Pharmacokinetic model

This model and the accompanying data were taken from [25]. A patient is given $D_{tot} = 48.15$ milligrams of a drug orally. The drug is absorbed into the blood stream at an assumed constant rate over a time $E_T$ (a parameter to be fit) so that the amount of drug that has entered the system after time $t$ (in
hours) is
\[
I(t) = \begin{cases} 
\frac{D_{\text{tot}}}{E_T} & \text{if } 0 \leq t < E_T, \\
D_{\text{tot}} & \text{if } E_T \leq t, 
\end{cases}
\] (49)
and the rate of absorption is
\[
I'(t) = \begin{cases} 
\frac{D_{\text{tot}}}{E_T} & \text{if } 0 \leq t < E_T, \\
0 & \text{if } E_T \leq t. 
\end{cases}
\]
At various times, blood concentrations of the drug \(D_b\) and also of its only metabolite \(M_b\) are measured (mg/l). The drug is transported between the blood and the tissue compartment, and both drug and metabolite leave the blood and enter the urine, where cumulative amounts are measured at various times. A simple mathematical model for this process is
\[
\begin{align*}
D'_b &= (I'(t) - (k_1 + \mu_D + k_M)D_b + k_2D_t) / V_b \\
M'_b &= (k_M D_b - \mu_M M_b) / V_b \\
D'_u &= \mu_D D_b \\
M'_u &= \mu_M M_b \\
D'_t &= (k_1 D_b - k_2 D_t) / V_t,
\end{align*}
\] (50)
where \(D_u\) and \(M_u\) are the cumulative amounts (mg) of drug and metabolite in the urine, and \(D_t\) is the concentration of drug in the tissue (mg/l). The model parameters are the rate constants \(k_1\) and \(k_2\) for the transport of drug between the blood and tissue compartments, the rate constant \(k_M\) for metabolism of the drug in the blood stream, the constants \(\mu_D\) and \(\mu_M\) that govern the rate of excretion of drug and metabolite from the blood to the urine, and \(V_b\) and \(V_t\), the effective volumes of the blood and tissue compartments. This system of
equations satisfies \((V_b(D_b + M_b)) + V_t D_t + D_u + M_u)' = I'(t)\). Hence, \(D_t\) can be given explicitly in terms of the other variables:

\[
D_t = \frac{I(t) - V_b(D_b + M_b) - (D_u + M_u)}{V_t}.
\]

Using (51) and defining a new parameter \(\kappa = k_2/V_t\), the five-dimensional system (50) becomes the following four-dimensional system with seven parameters (including \(E_T\)).

\[
\begin{align*}
D'_b &= I'(t) - (k_1 + \mu D + k_M)D_b + \kappa(I(t) - D_u - M_u) - \kappa(D_b + M_b) \\
M'_b &= \frac{k_MD_b - \mu MM_b}{V_b} \\
D'_u &= \mu DD_b \\
M'_u &= \mu MM_b
\end{align*}
\]

The data for this model are given in Table 8. Figure 11 shows a plot of these data together with the bands used to represent them continuously.

The original parameter box is given in Table 9; wide ranges were used for the rate constants since little \textit{a priori} information on them is available. The effective blood volume is constrained more closely at the start. After applying the five different unaccumulated discretizations \((w = 0)\) using step numbers \(s = 1\) to \(s = 14\) and various step sizes \(h\) ranging from 0.05 to 0.35, the discretization that gave the smallest \(\mu\) value \((\mu = 0.187)\) was A1OUT with \(s = 13\) and \(h = 0.1\). The hull of the consistent boxes (8,876 of 10,000) for this reduction was computed, and the resulting ranges for the parameters are given in Table 9. The range for
Table 8: Pharmacological data for the model given by (52) obtained from the web site of Civilized Software Inc.[25]. These data are attributed to Nicholas Holford of the Department of Pharmacology & Clinical Pharmacology, University of Auckland. The outliers for $M_b$ at times $t = 1.2$ and $t = 1.4$ were removed before fitting.

<table>
<thead>
<tr>
<th>$t$ (hours)</th>
<th>$D_b$ (mg/l)</th>
<th>$M_b$ (mg/l)</th>
<th>$D_u$ (mg)</th>
<th>$M_u$ (mg)</th>
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Table 9: Original parameter box and best hull of consistent boxes obtained by A1OUT with $s = 13$ and step size $h = 0.1$.

<table>
<thead>
<tr>
<th>$V_b$</th>
<th>$k_1$</th>
<th>$\kappa$</th>
<th>$k_M$</th>
<th>$\mu_D$</th>
<th>$\mu_M$</th>
<th>$E_T$</th>
</tr>
</thead>
<tbody>
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<td>[.01, 500]</td>
<td>[.01, 100]</td>
<td>[.01, 150]</td>
<td>[.01, 50]</td>
<td>[.01, 50]</td>
</tr>
<tr>
<td>best hull</td>
<td>[3, 7]</td>
<td>[.01, 500]</td>
<td>[.01, 6.26]</td>
<td>[37.5, 75.0]</td>
<td>[6.67, 12.9]</td>
<td>[9.66, 9.90]</td>
</tr>
</tbody>
</table>
μ_M was very small, while those for μ_D and κ were reasonably reduced. Some progress was made on the range for k_M (more progress would have been made if the algorithm were run longer, splitting more boxes), but no progress was made on V_b, k_1, and E_T. This is an indication that this small data set does not contain sufficient information to identify many of the parameters in the model. In particular there are no data for t < 0.82 and, as seen in Figure 11, the concentrations of D_b and M_b have essentially reached their peaks by this time. As expected, A1OUT was the best discretization followed closely by MAXORD, and distantly by B1OUT, FDF, and BDF. Values of μ for these discretizations for 1 ≤ s ≤ 14 and 0.05 ≤ h ≤ 0.35 are shown in Figure 12. The pattern displayed in this figure is precisely as expected given the values of A_0 for these discretizations.

As with the nonlinear pendulum model, the range reduction performance decreases for all of the discretizations as h is decreased while holding s constant (data not shown) due to the window length becoming too small compared to the height of the variable ranges. Moderate accumulation yields improved performance for BDF, FDF, and B1OUT, while mildly impairing the performance of A1OUT and MAXORD. Figure 13 shows the effect on μ as the accumulation index, w, is increased. The performance for the MAXORD discretization showed marked improvement when accumulated with w = ̂s, but for larger w, it steadily got worse, tracking very closely to the A1OUT performance. The improvement for BDF, FDF, and B1OUT with increased w can be attributed to the decrease in A_0 for these discretizations, which is significant until about s = ̂s + w = 60 (since A_0 is close to its limit by then). Again, the explanation for why all of the discretizations yield worse performance for larger w is not clear. Possibly, for this model and these data, when w is too large there aren’t enough sufficiently different large windows over the small data set to constrain the parameters well.
6. Conclusion

This paper considered the problem of identifying ranges for parameters in an ODE model that are consistent with time series data of the model variables. Five different discretization classes for ODEs were defined, and their use in a parameter range reduction algorithm were analyzed. For the prototypical model \( \dot{x} = \lambda x \), it was shown that the ranges obtained for \( \lambda \) were tightest with the A1OUT discretization class, followed closely by the MAX ORD class. The B1OUT, BDF, and FDF classes all generated considerably larger ranges. This result was shown largely to be a consequence of the value of \( A_0 \) (36) associated with each class. The value of \( A_0 \) was shown to have a minimum of 2, and this was achieved if and only if the discretization was in the A1OUT class. The other classes all had increasing values of \( A_0 \) as the step number \( s \) increased. Values of \( A_0 \) were especially large for the BDF, FDF, and B1OUT classes. The other requirement for good range reduction was that the overall window length \( L \) was sufficiently large compared to the noise (the height of the continuous band used to represent the data). Accumulation of any of these discretizations with a jump size of \( \delta = 1 \) and accumulation index \( w \geq \hat{s} \), resulted in decreasing \( A_0 \) values (except for A1OUT whose accumulated \( A_0 \) values were larger than for \( w = 0 \)) and consequently improved parameter range reduction. If the discretization was sign-separated, then in the limit as \( w \to \infty \), the value of \( A_0 \) approaches the minimum of 2.

These results for the simple model largely carried over to two more complicated models: a nonlinear pendulum with two equations and three parameters, and a pharmacokinetic model with four equations and seven parameters. The primary difference noted for these more complicated models was that accumulation was only beneficial until \( s = \hat{s} + w \) was about ten times the size of \( \hat{s} \). Beyond that, further accumulation had a detrimental effect. For the pharmacokinetic model, this possibly is attributed to the small data set.
The conclusion is that the A1OUT class of discretizations with moderate accumulation probably is the best discretization to use in the parameter range reduction scheme.

The parameter range reduction scheme restricts itself to discretization windows over which the vector field is monotonic with respect to the parameters. This facilitates rapid and efficient computation of the range $F$ of the discretization. In some situations however, this restriction excludes portions of the data set from contributing to the reduction process. In this case, the scheme could be modified to calculate $F$ using either interval arithmetic methods or an optimization technique, but this would increase the computation time. Nonetheless, the possible gain in information may make that an acceptable price. The results from Section 4 should still be applicable under such a modification since they are based on exact bounds for the ranges for the prototypical model: A1OUT discretizations should continue to provide greatest range reduction.

This parameter range reduction scheme has some advantages compared to other parameter identification techniques. The fact that its output is a set of boxes in parameter space, as opposed to a single point estimate, provides additional information. Wide dimensions of the output boxes correspond to parameters whose values do not greatly affect the model (in relation to the data), while narrow dimensions correspond to parameters to which the model is very sensitive. The overall size of the output boxes is an indication of how much information is in the data. If the set of output boxes in the $q$-dimensional parameter space is aligned along a $k$-dimensional submanifold, $k < q$, then this is an indication that the model is overly complex in relation to the information in the data. At least theoretically, it should be possible to combine $k$ of the parameters into one and still achieve equally good fits to the data. This kind of information is useful to the modeller since it helps in the determination of an appropriate model form. For the experimentalist, this information isolates the parameters that are not well identified by the data, and may suggest the types of experiments that are needed to yield data that would discriminate them.

References


