COMPUTING HOPF BIFURCATIONS II: THREE EXAMPLES FROM NEUROPHYSIOLOGY

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Abstract. In a previous paper [11] we presented algorithms for detecting Hopf bifurcations in two-parameter families of vector fields based on classical algebraic constructions. In addition to their utility as augmented systems for use with standard Newton-type continuation methods, they were shown to be particularly well-adapted for solution by computer algebra techniques for vector fields of small or moderate dimension. The present study examines the performance of these methods on test problems selected from models of current research interest in neurophysiology. Implementation issues are examined and the numerical properties of the proposed methods are compared with several alternative algorithms for Hopf pathfollowing that appear in the literature.

Key words. Hopf bifurcation, resultant, bialternate product, neuron model

AMS subject classifications. 58F14, 65H17, 92-08, 92C20

1. Introduction. The onset of small amplitude oscillations in dynamical systems occurs at Hopf bifurcations. The simplest version of the Hopf Theorem is the following:

THEOREM 1.1. *Let*

$$\dot{x} = f(x,\mu) \qquad f : \mathbb{R}^n \times \mathbb{R}^k \to \mathbb{R}^n \tag{1}$$

be a smooth n-dimensional vector field depending upon k parameters with the property that (x_0, μ_0) is an equilibrium point at which the Jacobian matrix $D_x f$ has no zero eigenvalues and a single, simple pair of pure imaginary eigenvalues $\lambda, \bar{\lambda}$. Assume further that $\lambda, \bar{\lambda}$ cross the imaginary axis transversally as the parameters μ are varied. Then there is a smooth submanifold P of dimension $k+1$ containing (x_0, μ_0) that is a union of periodic orbits and equilibrium points of f.

We are concerned with the numerical *detection* of Hopf bifurcation points. This constitutes location of values (x, μ) at which $f(x, \mu) = 0$ and $Df(x, \mu)$ has a pair of pure imaginary eigenvalues. Several methods for computing such points have been proposed and implemented by various authors (For recent reviews, see [18, 24]).

To motivate the discussion that follows, we begin by considering the following planar vector field:

$$\begin{aligned} \dot{x} &= \gamma\left(x + y - x^3/3 + \xi\right) \\ \dot{y} &= -(x - \alpha + \beta y)/\gamma \end{aligned} \tag{2}$$

This model for the propagation of electrical impulses along a nerve axon was proposed by Fitzhugh [6] as a tractable simplification of the more complicated Hodgkin-Huxley equations discussed as the first example in Section 2. Equilibrium points for equations (2) are points which satisfy $\dot{x} = \dot{y} = 0$. Hopf bifurcation points are determined by the Jacobian at the equilibrium. They occur where the trace $\beta/\gamma - \gamma(1 - x^2)$ is zero and the determinant $1 - \beta(1 - x^2)$ is positive. Thus the determination of Hopf bifurcation points for Equation (2) described above can be written as the following problem:

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Problem (P1):

Find: $(\hat{x}, \hat{y})$ and $(\alpha, \beta, \gamma, \xi)$

Satisfying:

$$\begin{pmatrix} \gamma\left(x + y - x^3/3 + \xi\right) \\ -\left(x - \alpha + \beta y\right) \\ \beta/\gamma - \gamma(1 - x^2) \end{pmatrix} = 0$$

Subject To:

$$1 - \beta(1 - x^2) > 0$$

We seek to extend the approach to detecting Hopf bifurcations in this example to vector fields of higher dimension. We need a non-linear system of equations comprised of the equilibrium condition of Equation (1) and the algebraic criteria that determine when the Jacobian matrix has a single pair of pure imaginary, conjugate eigenvalues in its spectrum. In [11] we discuss classical algebraic constructions for determining matrices of arbitrary dimension with pure imaginary eigenvalues. A single equality condition and an inequality in the coefficients of the characteristic polynomial are formulated in terms of *resultants*, determinants of special matrices whose elements are functions of the characteristic polynomial coefficients. The equality condition is also derived directly from the Jacobian as the determinant of a *bialternate product* (biproduct) matrix constructed from the Jacobian entries. The biproduct matrix is generally sparse and block-structured. Thus, in arbitrary dimensions the non-linear rootfinding problem corresponding to that of (P1) can be expressed in terms of the defining equations for the vector field and the Jacobian elements alone. We note that there is some overlap in our approach with work of previous authors. In particular, the program *LINLBF* by Khibnik and his coworkers [15] incorporates a method for following curves of Hopf bifurcations based on the resultant of two polynomials which is similar to that used here. In [11] we extend their work by examining several variations of the resultant methods which have differing numerical properties and derive the inequality condition that makes identification of the Hopf points possible. The biproduct formulation is new as is the formulation of conditions under which regularity holds.

Here we discuss the implementation of our new methods, describe their application to three examples from neurophysiology and make comparisons with other approaches to computing Hopf bifurcations. Each of the examples that we describe comes from a neurophysiological model for the electrical activity of a neuron and each illustrates a different aspect of the methods. In some other problems of modest size or special structure, computer algebra programs produce curves of Hopf bifurcations analytically. However, given an arbitrary nonlinear vector field, solving for the roots of the required system of equations is generally infeasible in closed-form. One can attempt to solve (P1) numerically and to follow curves of Hopf bifurcation points in two-parameter families of vector fields. In [11] we showed that these augmented systems do, indeed, satisfy the properties required for use in Newton-type numerical continuation.

Our goal in examining these algorithms has been to develop computational methods that facilitate the comparison of biologically-based neural models with experimental data. In the first example of Section 2, we illustrate the application of symbolic methods to the detection of Hopf bifurcations in the classical Hodgkin-Huxley model

for action potentials of a squid giant axon. We also use the Hodgkin-Huxley example to compare the accuracy of numerical calculations of derivatives using 'automatic differentiation' with finite difference techniques and analytic evaluation. The second example shows the performance of the resultant approach on a more complex model for the electrical activity of a bursting neuron. This model contains a point of double Hopf bifurcation in its parameter space. We make a detailed comparison of our algorithms with other strategies for detecting Hopf bifurcations for this model. The third example is a still larger and stiffer system of differential equations formulated as a model for electrical activity of a stomatogastric neuron of the crab, *Cancer borealis*. We examine the problems caused in the detection of Hopf bifurcations by large eigenvalues in the linearization of this model.

The paper is organized into two sections. The first section is a review of methods for detecting Hopf bifurcations, including those discussed in [11]. The second section presents results obtained for the three examples, beginning with a brief description of the biological origins of each model. We conclude with a summary of our experiments and discuss directions for future work.

2. Review of Hopf Bifurcation Algorithms.

2.1. Minimally Augmented Systems. In this section we review strategies for detecting curves of Hopf bifurcation points in two parameter families of vector fields. We consider first methods based on the algebra of polynomial resultants in families of autonomous vector fields of the form

$$\dot{x} = f(x, \alpha; \beta) \tag{3}$$

where $f : D \subset \mathbb{R}^n \times \mathbb{R} \times I \to \mathbb{R}^n$ and $\beta \in I \subset \mathbb{R}$. For simplicity, we distinguish the second parameter by considering both $x(\beta)$ and $\alpha(\beta)$ to be functions of β. The Jacobian matrix of the vector field is given by

$$\mathbf{J} \equiv \mathbf{J}(x, \alpha; \beta) = \frac{\partial f}{\partial x}(x, \alpha; \beta) \quad .$$

$\mathbf{J}$ defines a map from the product space of phase and parameter variables to the space of n-square matrices, denoted by $\mathcal{M}$.

Direct methods for computing curves of Hopf bifurcation for Equation (3) involve appending a determining equation that vanishes when $\mathbf{J}$ has pure imaginary eigenvalues to the equilibrium equations $f(x, \alpha; \beta) = 0$. Thus, we seek a C^2-smooth function $g : \mathbb{R}^n \times \mathbb{R} \times \mathbb{R} \to \mathbb{R}^{n+1}$ so that the *augmented* system:

$$F(x, \alpha; \beta) = \begin{pmatrix} f(x, \alpha; \beta) \\ g(x, \alpha; \beta) \end{pmatrix} \tag{4}$$

vanishes at a point of Hopf bifurcation. Furthermore, we require that a point of Hopf bifurcation $(x^*, \alpha^*; \beta^*)$ be a regular solution of Equation (4).
If the characteristic polynomial of $\mathbf{J}$ is given by

$$p(\lambda) = c_0 + c_1\lambda + \cdots + c_{n-1}\lambda^{n-1} + \lambda^n \quad .$$

then p has the non-zero root pair $\{\lambda, -\lambda\}$ if and only if λ is a common root of the two equations $p(\lambda) + p(-\lambda)$ and $p(\lambda) - p(-\lambda)$. Making the substitution $z = \lambda^2$ and rearranging, we construct two new polynomials. If n is even, let

$$
\begin{aligned}
r_e(z) &= c_0 + c_2 z + c_4 z^2 + \cdots + c_{n-2} z^{\frac{n-2}{2}} + z^{\frac{n}{2}} \\
r_o(z) &= c_1 + c_3 z + c_5 z^2 + \cdots + c_{n-1} z^{\frac{n-2}{2}}
\end{aligned} \tag{5a}
$$

while if n is odd, set

$$
\begin{aligned}
r_e(z) &= c_0 + c_2 z + c_4 z^2 + \cdots + c_{n-3} z^{\frac{n-3}{2}} + c_{n-1} z^{\frac{n-1}{2}} \\
r_o(z) &= c_1 + c_3 z + c_5 z^2 + \cdots + c_{n-2} z^{\frac{n-3}{2}} + z^{\frac{n-1}{2}}
\end{aligned} \tag{5b}
$$

Then p has a non-zero root pair $\{\lambda, -\lambda\}$ if there exists a z that satisfies:

$$
\begin{pmatrix} r_e(z) \\ r_o(z) \end{pmatrix} = \mathbf{0} \ .
$$

Two polynomials have a common root if and only if they share a common factor. There are several equivalent ways of determining whether two univariate polynomials have a common root. First, the Euclidean algorithm yields a sequence of polynomials of decreasing degree that are in the ideal generated by $r_e(z)$ and $r_o(z)$. The last term in this sequence can be expressed as a determinant constructed from the coefficients of two polynomials. We describe one way to do so.

The *Bezout* resultant is a determinant that indicates whether r_e and r_o have a common root. For n even, consider the two polynomials specified by Equation (5a). We define the brackets

$$
[i, j] = det \begin{bmatrix} c_{2i} & c_{2j} \\ c_{2i+1} & c_{2j+1} \end{bmatrix}
$$

where $0 \leq i, j \leq \frac{n}{2}$ and we take $c_n = 1, c_{n+1} = 0$. The *Bezout* matrix, $\mathcal{B}$, corresponding to the polynomial pair (r_e, r_o) is an $\frac{n}{2}$-dimensional square, symmetric matrix with entries constructed as sums of brackets in the coefficients c_i as follows: For $1 \leq i \leq j \leq \frac{n}{2}$ set

$$
\begin{aligned}
k_{min} &= max(0, i + j - n/2 - 1) \\
k_{max} &= i - 1
\end{aligned} \tag{6}
$$

$$
(\mathcal{B})_{ij} = \sum_{k=k_{min}}^{k_{max}} [i + j - k - 1, k] = (\mathcal{B})_{ji} \ . \tag{7}
$$

The only modification required in this definition for the case of n odd is that c_n has the value prescribed by the characteristic polynomial, p, and c_{n+1} is taken to be unity. We also define the *Bezout subresultants* $\mathcal{B}_0$ and $\mathcal{B}_1$ as the determinants of the matrices obtained from $\mathcal{B}$ by deleting the first column and the i^{th} row of $\mathcal{B}$. The following theorem is proved in [11].

THEOREM 2.1. *Let B be the Bezout matrix for the polynomials r_e and r_o in Equation (2). Then* $\mathbf{J}$ *has precisely one pair of pure imaginary eigenvalues if*

$$
det(\mathcal{B}) = 0 \quad and \quad det(\mathcal{B}_0) \cdot det(\mathcal{B}_1) > 0.
$$

If $det(\mathcal{B}) \neq 0$ or $det(\mathcal{B}_0) \cdot det(\mathcal{B}_1) < 0$, then $p(\lambda)$ has no pure imaginary roots.

Table 1 provides a list of the resultant equality and subresultant inequality conditions, as functions of the polynomial coefficients, for vector fields of dimension two to six.

TABLE 1

Resultant equality and subresultant inequality conditions required for Hopf bifurcation for vector fields of dimension two through six.

n	$det(\mathcal{B})$ $det(\mathcal{S}_0) \cdot det(\mathcal{S}_1)$
2	c_1
	c_0
3	$c_0 - c_1c_2$
	c_1
4	$c_0c_3^2 - c_1c_2c_3 + c_1^2$
	c_1c_3
5	$(c_2 - c_3c_4)(c_1c_2 - c_0c_3) + c_1c_4(c_1c_4 - 2c_0) + c_0^2$
	$(c_2 - c_3c_4) \cdot (c_0 - c_1c_4)$
6	$c_0c_5^2(c_0c_5 - c_2c_3) + c_1c_5^2(c_2^2 - c_0c_4) + c_1(c_1^2 + c_0c_3c_5) + c_1c_5(c_0c_3 - 2c_1c_2) + (c_4c_5 - c_3)(c_0c_3^2 - c_0c_1c_5 + c_1^2c_4 - c_1c_2c_3)$
	$(c_1c_3 + c_0c_5^2 - c_1c_4c_5) \cdot (c_3^2 - c_1c_5 + c_2c_5^2 - c_3c_4c_5)$

To circumvent possible difficulties in explicitly determining the characteristic polynomial coefficients of $\mathbf{J}$, we described a method for determining whether a square matrix has a pair of eigenvalues with zero sum directly from the entries in the Jacobian matrix.

Definition: Let $\mathbf{A}$ and $\mathbf{B}$ be $n \times n$ matrices with entries (a_{ij}) and (b_{ij}), respectively, $1 \leq i, j \leq n$. Set $m = \frac{n}{2}(n-1)$. Then the *bialternate product* (or biproduct) of $\mathbf{A}$ and $\mathbf{B}$, denoted $\mathbf{A} \odot \mathbf{B}$, is an $m \times m$ matrix whose rows are labeled pq for $(p = 2, 3, \cdots, n; q = 1, 2, \cdots, p-1)$ and columns labeled rs, $(r = 2, 3, \cdots, n; s = 1, 2, \cdots, r-1)$ with entries

$$(\mathbf{A} \odot \mathbf{B})_{\{pq,rs\}} = \frac{1}{2}\left\{ \begin{vmatrix} a_{pr} & a_{ps} \\ b_{qr} & b_{qs} \end{vmatrix} + \begin{vmatrix} b_{pr} & b_{ps} \\ a_{qr} & a_{qs} \end{vmatrix} \right\}.$$

THEOREM 2.2. *Let* $\mathbf{A}$ *be an* $(n \times n)$ *matrix with eigenvalues* $(\lambda_1, \cdots, \lambda_n)$. *Then*

(i) $\mathbf{A} \odot \mathbf{A}$ *has eigenvalues* $\lambda_i \cdot \lambda_j$, *and*
(ii) $2\mathbf{A} \odot \mathbf{I}_n$ *has eigenvalues* $\lambda_i + \lambda_j$

where $\mathbf{I}_n$ *is the n-square identity matrix and* $1 \leq j < i \leq n$.

Substituting $\mathbf{I}_n$ into the definition of the bialternate product and solving for the elements yields a simple formula for the entries. For the $\frac{n}{2}(n–1)$-square matrix $2\mathbf{A} \odot \mathbf{I}_n$ with rows, pq, and columns, rs, the entries are given by the formula,

$$(8)\qquad (2\mathbf{A}\odot\mathbf{I}_n)_{\{pq,rs\}} = \begin{cases} -(A)_{ps} & \text{if } r=q \\ (A)_{pr} & \text{if } r\neq p \text{ and } s=q \\ (A)_{pp}+(A)_{qq} & \text{if } r=p \text{ and } s=q \\ (A)_{qs} & \text{if } r=p \text{ and } s\neq q \\ -(A)_{qr} & \text{if } s=p \\ 0 & \text{otherwise} \end{cases}$$

From the algebraic theory of symmetric matrix products described above we have a simple *necessary* condition for a Hopf point: If the point (x^*, λ^*) is a Hopf bifurcation point for $\dot{x} = f(x, \alpha)$, then the $(n+1)$-dimensional system

$$(9)\qquad F(x^*,\alpha^*) = \begin{pmatrix} f(x^*,\alpha^*) \\ det\left(D_x f \odot \mathbf{I}_n\big|_{(x^*,\alpha^*)}\right) \end{pmatrix}$$

vanishes. However, we have not found a condition that distinguishes pure imaginary eigenvalues from real pairs with zero sum directly from the Jacobian and its bialternate products in analogy to the subresultant criteria described earlier.

Both the determinant of the biproduct and the resultant provide augmentation functions g that can be used in detecting Hopf bifurcations in one parameter families of vector fields or in applying continuation methods for the computation of curves of Hopf bifurcations in two parameter families. The regularity theorem of [11] guarantees that the matrix of partial derivatives of the augmented system $F = 0$ has maximum rank $n + 1$ at points of simple Hopf bifurcation. In Section 2, we discuss several aspects of standard root finding and continuation methods that can be improved by taking into account the nature of the augmenting function g.

2.2. Other Methods Based on the Characteristic Polynomial. Kubiček has previously described two direct methods for computing Hopf bifurcation points which require explicitly the coefficients of a matrix characteristic polynomial [16, 17]. Both methods result in $(n+2)$-dimensional systems of algebraic equations which may be solved by conventional continuation techniques. Performance of these algorithms has been evaluated on a variety of testcases, including panel flutter and non-adiabatic tubular reactions [24], continuous-stirred tank reactions [13] and parabolic reaction-diffusion equations [23] with favorable results.

The two methods of Kubiček are based on the direct determination of the pure imaginary eigenvalues, say $\lambda^*_{1,2} = \pm\sqrt{\omega}i$, of the Jacobian characteristic polynomial, p. Suppose such an eigenvalue pair exists. Then there is a polynomial, q, of degree $(n-2)$ such that

$$\begin{aligned} p(\lambda) &= (\lambda^2+\omega)q(\lambda) \\ &= (\lambda^2+\omega)\sum_{k=0}^{n-2} b_k\lambda^{n-k-2} + A\lambda + B \end{aligned}$$

where the b_i are given recursively by the formula $b_i = c_i - \omega b_{i-2}$ for $1 \le i \le n-2$ with $b_{-1} = 0$. We require the constant and linear coefficients, A and B to be zero; that is,

$$(10)\qquad \begin{pmatrix} A(x,\alpha) \\ B(x,\alpha) \end{pmatrix} = \begin{pmatrix} c_{n-1} - \omega b_{n-3} \\ c_n - \omega b_{n-2} \end{pmatrix} = \mathbf{0}$$

where the dependence of A and B on (x, α) has been emphasized. Thus, Equation (10) yields a 2-dimensional augmented system which must vanish at a Hopf bifurcation point:

$$F(x, \alpha, \omega) = \begin{pmatrix} f(x, \alpha) \\ c_{n-1} - \omega b_{n-3} \\ c_n - \omega b_{n-2} \end{pmatrix} \qquad (K1)$$

Kubiček's second method depends on the observation that if (x^*, α^*) is a point of Hopf bifurcation with imaginary eigenvalues $\pm\sqrt{\omega}i$, then the matrix $\mathbf{J}^2$ has a real eigenvalue, $-\omega$, with multiplicity equal to two. Suppose the characteristic polynomial of $\mathbf{J}^2$ has r eigenvalues distinct from $-\omega$; that is, we take the spectrum of $\mathbf{J}^2$ to be $\{-\omega, \lambda_1, \cdots, \lambda_r\}$, with respective multiplicities $\{m_\omega, m_1, \cdots, m_r\}$ where $(m_\omega + m_1 + \cdots m_r) = n$. Then q may be written,

$$q(\lambda) = (\lambda + \omega)^{m_\omega} \prod_{k=0}^{r} (\lambda - \lambda_k)^{m_k} \quad . \qquad (11)$$

Differentiating with respect to λ we obtain,

$$\frac{dq}{d\lambda} = m_\omega (\lambda + \omega)^{m_\omega - 1} \prod_{k=0}^{r} (\lambda - \lambda_k)^{m_k} + (\lambda + \omega)^{m_\omega} \frac{d}{d\lambda} \prod_{k=0}^{r} (\lambda - \lambda_k)^{m_k}$$

For $-\omega$ to be a double real root,

$$q(-\omega) = 0 = \frac{dq}{d\omega}(-\omega)$$

which leads to the augmented system,

$$F(x, \alpha, \omega) = \begin{pmatrix} f(x, \alpha) \\ q(-\omega) \\ \frac{dq}{d\omega}(-\omega) \end{pmatrix} \quad . \qquad (K2)$$

2.3. Other Methods Not Based on the Characteristic Polynomial. Here we review methods for computing Hopf bifurcations which do not require the coefficients of the Jacobian characteristic polynomial. Most of the methods in this category use variants of two distinct defining equations. Our discussion summarizes the main features of these methods; for more details see Roose [22].

Suppose (x^*, α^*) is a Hopf bifurcation point for Equation (2) with pure imaginary eigenvalues $\pm\omega i$ and associated eigenvector $u + vi$. Denote $E = span(u, v)$, which is two-dimensional if $\mathbf{J}$ is non-singular. The defining relation,

$$(D_x f - \omega \mathbf{I})(u + vi) = 0$$

leads to the augmented system

$$F_1(x, \alpha, u, v, \omega) = \begin{pmatrix} f(x, \alpha) \\ [D_x f]\, u - \omega v \\ [D_x f]\, v + \omega u \\ \mathcal{N}(u, v) \end{pmatrix} \quad .$$

If the same construction is applied to the matrix $\mathbf{J}^2 = [D_x f]^2$, we obtain the inflation

$$F_2(x, \alpha, u, \omega) = \begin{pmatrix} f(x, \alpha) \\ [D_x f]^2 u + \omega^2 u \\ \mathcal{N}(u) \end{pmatrix} \quad .$$

The operator $\mathcal{N} : X \to \mathbb{R}^2$, where X is either $\mathbb{R}^n \times \mathbb{R}^n$ or $\mathbb{R}^n$, is used to normalize the vectors u and v and typically requires a fixed vector l. Precisely how l is selected is a matter of implementation, but it must be chosen so that $l \notin E$. Two choices for $\mathcal{N}$ have been discussed extensively in the literature. Griewank and Reddien [9] suggested the use of

$$\mathcal{N}_1 = \begin{pmatrix} < l, u > \\ < l, v > -1 \end{pmatrix}$$

in conjunction with F_1 and showed that both Hopf and simple quadratic turning points are regular, isolated solutions to the system of equations. An alternative proposed by Roose and Hlavacek [22] is to take

$$\mathcal{N}_2 = \begin{pmatrix} < l, u > \\ < v, v > -1 \end{pmatrix}$$

which, for l chosen as prescribed above, does not admit turning points as isolated solutions.
Each of the four possible choices available by this construction can be used with standard continuation techniques to track curves of Hopf bifurcation in two-parameter families. For example, if we set $y = (x, \alpha, u, v, \omega)$, then the k^{th} Newton step taken to find a local root $F_1(y) = 0$ will require the solution of the linearized system,

$$y_{k+1} = y_k - [D_y F_1(y_k)]^{-1} F_1(y_k) \quad .$$

While it is possible to ignore the special structure of $D_y F(y_k)$ and solve for the updated step with LU decomposition, much faster algorithms may be obtained by exploiting the block structure of the Jacobian for the augmented system. Computer software designed to implement general-purpose numerical bifurcation techniques must be specially modified to accommodate these special Newton-step solution methods.

3. Three Examples.

3.1. Hodgkin/Huxley Equations. The space-clamped Hodgkin/Huxley equations are a system of four nonlinear ordinary differential equations that describe the electrical response of the giant nerve axon from the squid *Loligo* to an externally-applied current [14]. The typical response of the axon to a step in the stimulus current, I, is characterized by an abrupt spike in the electrical potential difference, v, between the intracellular fluid and the extracellular medium called an *action potential*. In the Hodgkin/Huxley model this depolarization is induced primarily by an inward flux of sodium (Na^+) followed by an outward flow of potassium (K^+) ions. Other ions contribute to a "leak" current across the axon membrane. The sodium and potassium currents are controlled by three *gating* variables denoted m, n and h, together with parameters, $\bar{g}_{Na}$, $\bar{g}_K$ and $\bar{g}_l$ that measure the maximum conductances of the channels. The resulting vector field is given by:

TABLE 2

Summary of the defining equations for the direct methods discussed in the paper for use with pathfollowing numerical codes. Labels are used in the sequel to distinguish the various algorithms.

Label	$g : \mathbb{R}^n \times \mathbb{R}^m \times \mathbb{R} \times \mathbb{R} \to \mathbb{R}^l$	m	l
RS,RB	$g(x,\alpha;\beta) = det(\mathcal{B})(x,\alpha;\beta)$	0	1
BP	$g(x,\alpha;\beta) = det\left([D_x f] \odot I_n\right)$	0	1
JGR	$g(x,v,w,\omega,\alpha;\beta) = \begin{pmatrix} [D_x f]\, v - \omega w \\ [D_x f]\, w + \omega v \\ < v, w > -1 \\ < l, v > \end{pmatrix}$	$2n+1$	$2n+2$
RH	$g(x,w,\omega,\alpha;\beta) = \begin{pmatrix} [D_x f]^2\, w - \omega^2 w \\ < w, w > -1 \\ < l, w > \end{pmatrix}$	$n+1$	$n+2$
K1	$g(x,\omega,\alpha;\beta) = \begin{pmatrix} c_{n-1} - \omega b_{n-3} \\ c_n - \omega b_{n-2} \end{pmatrix}$	1	2
K2	$g(x,\omega,\alpha;\beta) = \begin{pmatrix} q(-\omega) \\ \frac{dq}{d\omega}(-\omega) \end{pmatrix}$	1	2

$$
\begin{aligned}
\dot{v} &= -G(v,m,n,h) - I \\
\dot{m} &= \Phi(T)\left[(1-m)\alpha_m(v) - m\beta_m(v)\right] \\
\dot{n} &= \Phi(T)\left[(1-n)\alpha_n(v) - n\beta_n(v)\right] \\
\dot{h} &= \Phi(T)\left[(1-h)\alpha_h(v) - h\beta_h(v)\right]
\end{aligned} \tag{12}
$$

where $\dot{x}$ stands for dx/dt and Φ is given by $\Phi(T) = 3^{(T-6.3)/10}$. The other functions involved are

$$G(v,m,n,h) = \bar{g}_{\rm na} m^3 h (v - \bar{v}_{\rm na}) + \bar{g}_{\rm k} n^4 (v - \bar{v}_{\rm k}) + \bar{g}_{\rm l}(v - \bar{v}_{\rm l})$$

and the equations modeling the variation of membrane permeability:

$$
\begin{array}{llll}
\alpha_m(v) = \Psi((v+25)/10) & & \beta_m(v) = 4e^{v/18} \\
\alpha_n(v) = \frac{1}{10}\Psi((v+10)/10) & & \beta_n(v) = 0.125e^{v/80} \\
\alpha_h(v) = 0.07e^{v/20} & & \beta_h(v) = \left(1 + e^{(v+30)/10}\right)^{-1} \\
\Psi(x) = x/(e^x - 1) & &
\end{array}
$$

We use the temperature $T = 6.3°\mathrm{C}$ and parameter values for $\bar{g}_{\rm ion}$ and $\bar{v}_{\rm ion}$ used by Hodgkin and Huxley [14]:

$$
\begin{array}{lll}
\bar{g}_{\rm na} = 120\mathrm{mS/cm}^2 & \bar{g}_{\rm k} = 36\mathrm{mS/cm}^2 & \bar{g}_{\rm l} = 0.3\mathrm{mS/cm}^2 \\
\bar{v}_{\rm na} = -115\mathrm{mV} & \bar{v}_{\rm k} = 12\mathrm{mV} & \bar{v}_{\rm l} = 10.599\mathrm{mV}
\end{array}
$$

The space-clamped Hodgkin-Huxley equations exhibit periodic solutions that arise through Hopf bifurcation with varying (v_k, I) [21]. In general, one does not expect to be able to find explicit analytic expressions for the solutions to multi-dimensional systems of equations, but the special structure of the Hopf bifurcation points allows us to do so. All the Hopf data reported in the discussion which follows was computed using the Maple© symbolic algebra package, reproduced using the same approach in Mathematica© and verified by standard numerical continuation using the augmented systems (GR1) and (R1) described in Section 3.2.

The Jacobian matrix corresponding to Equations (12), tedious to derive by hand, is found easily in Maple©. The corresponding characteristic polynomial

$$p(\lambda) = \lambda^4 + \sum_{i=0}^{3} c_i(v, m, n, h; v_k, I) \cdot \lambda^i$$

may be formed and the expressions required by Theorem 2.1 follow by inspection:

$$det(\mathcal{B}) = c_0 c_3^2 - c_1 c_2 c_3 + c_1^2 \tag{13a}$$

$$det(\mathcal{B}_0) \cdot det(\mathcal{B}_1) = c_1 \cdot c_3 \tag{13b}$$

The locus of Hopf bifurcation points in the (v_k, I) plane will be computed as a curve parameterized by v^*, the equilibrium values of v. Suppose that, for a prescribed v_k and I, the point (v^*, m^*, n^*, h^*) is an equilibrium for Equations (12). Since the equations for $\dot{m}$, $\dot{n}$ and $\dot{h}$ depend linearly on m,n and h,

$$\begin{aligned} m^* &= \frac{\alpha_m(v^*)}{\alpha_m(v^*) + \beta_m(v^*)} \\ n^* &= \frac{\alpha_n(v^*)}{\alpha_n(v^*) + \beta_n(v^*)} \\ h^* &= \frac{\alpha_h(v^*)}{\alpha_h(v^*) + \beta_h(v^*)} \end{aligned} \tag{14}$$

Observe that Equations (14) are independent of I and v_k and have non-zero denominators. Therefore, we obtain equilibrium values of m^*, n^* and h^* to be used in calculating I and v_k. The Jacobian of Equations (12) is independent of I and Equation (13a) depends quadratically on v_k. Therefore, we can solve Equation (13a) for values $v_k^{\pm}(v^*)$ yielding Hopf bifurcation at the equilibrium (v^*, m^*, n^*, h^*). Finally, substitution of the equilibrium coordinates and the values $v_k^{\pm}(v^*)$ into Equations (12), gives the value of $I = -G$ at the point of Hopf bifurcation. Algorithm 1 summarizes the steps required to compute Hopf bifurcation points in the (v_k, I) parameter plane.

For nominal values of the other system parameters, there is a single, connected curve of Hopf bifurcation points in the rectangular region $[-45, 130]$ mV $\times$ $[-150, 400]$ mA of the (v_k, I) plane. Table 3 lists the phase and parameter space coordinates of nineteen selected points used for comparison in the discussion that follows. In particular, points one and nineteen are chosen near Takens-Bogdanov bifurcations which lie at either terminus of the Hopf curve. The curve of Hopf points exhibits a narrow turning point with respect to the stimulus current, I, near one end. Points one through ten resolve the turning point of the Hopf curve.

We give a brief comparison of methods for computing the partial derivatives of augmenting functions using this example. For what follows, let $y = (v, m, n, h, v_k)$ denote the vector of phase space variables augmented with the parameter v_k and

procedure hh_hopf

3.0 Choose v^*.

3.1 Evaluate m^*, n^* and h^* *symbolically.*

3.2 Substitute m^*, n^* and h^* expressions into Hopf determining conditions and simplify to form $v_k^{\pm}(v^*)$.

3.3 Check the sign of the subresultant condition.

3.4 Evaluate $G^{\pm}(v^*)$ and solve for $I = -G(v^*, m^*, n^*, h^*)$.

return $\{v_i^*, m_i^*, n_i^*, h_i^*\}$

ALGORITHM 1

Procedure for computing Hopf bifurcation points in Maple given a value for the external current, I.

TABLE 3

Phase and parameter space coordinates for the selected points in the Hopf curve. Points one through ten lie near a Takens-Bogdanov point at one end of the Hopf curve. The last column shows the computed magnitude of the pure imaginary eigenvalue.

Pt	v	m	n	h	v_k	I	$Im(\lambda)$
1	-23.072	0.44955	0.65670	0.06213	-30.34	-100.80	0.0097
2	-23.122	0.45089	0.65729	0.06178	-30.42	-101.35	0.0664
3	-23.179	0.45239	0.65795	0.06140	-30.50	-101.88	0.0985
4	-23.257	0.45445	0.65886	0.06088	-30.58	-102.41	0.1338
5	-23.340	0.45666	0.65983	0.06033	-30.61	-102.65	0.1679
6	-23.457	0.45977	0.66118	0.05957	-30.55	-102.15	0.2153
7	-23.499	0.46089	0.66167	0.05929	-30.47	-101.62	0.2332
8	-23.529	0.46168	0.66201	0.05910	-30.40	-101.09	0.2465
9	-23.556	0.46239	0.66232	0.05893	-30.31	-100.48	0.2589
10	-23.573	0.4628	0.6625	0.0588	-30.243	-100.0	0.2673
11	-23.700	0.4662	0.6640	0.0580	-23.112	-50.0	0.5497
12	-23.422	0.4588	0.6608	0.0598	-15.660	0.0	0.6974
13	-23.042	0.4487	0.6563	0.0623	-7.764	50.0	0.8197
14	-22.590	0.4368	0.6510	0.6550	0.6947	100.0	0.9316
15	-19.798	0.3641	0.6165	0.0894	45.629	300.0	1.3894
16	-12.032	0.1923	0.5068	0.2124	119.294	300.0	1.9024
17	-7.056	0.1169	0.4290	0.3494	76.506	100.0	1.3727
18	-6.036	0.1048	0.4128	0.3829	42.543	50.0	1.0091
19	-4.225	0.0860	0.3839	0.4453	-5.1060	0.0	0.0612

$g(\cdot)$ the function for Hopf detection. We consider here the augmenting function (BP) of Table 2, given by $g(y; I) = det\,(2\mathbf{J} \odot \mathbf{I}_n)$. Recall that the standard Newton-type corrector step requires the solution of a linear system, the matrix of which contains partial derivatives of the form $\frac{\partial}{\partial y_l} g(y)$. As in most examples, we cannot determine exactly the values of the relevant partial derivatives at arbitrary points along the Hopf branch. Our objective here is to compare the common techniques for computing derivatives as applied to the Hodgkin/Huxley equation, and comment on their distinguishing characteristics. The Hodgkin/Huxley equations are well-suited to this

comparison because expressions for the higher-order derivatives of the defining equations, although lengthy, may be easily formed. For example, values for the partial derivatives $\frac{\partial}{\partial v}(2\mathbf{J} \odot \mathbf{I}_4)$ may be computed using the adjoint formula given in [11]. Table 4 shows a compilation of these partial derivatives, computed for point 14 of Table 3. In our experiments, the adjoint matrix was formed in a general fashion, using determinants computed using LU factorization of appropriate submatrices.

TABLE 4

Values of partial derivatives $\frac{\partial g}{\partial v}$ and $\frac{\partial g}{\partial m}$ where $g = det(2\mathbf{J} \odot \mathbf{I}_4)$. Data is presented for partials computed by automatic differentiation (AD), the adjoint formula of Section 2.4 (AF), forward differencing (FD) and central differencing (CD). Each entry associated to a difference formula is followed by the mantissa of the stepsize.

Meth	v		m	
AD	-54.2506431900141592		-7728.29850144535158	
AF	-54.250643190015		-7728.298501445353	
CD	-54.250643 2	(-4)	-7728.298501 5	(-6)
FD	-54.25063	(-6)	-7728.29853	(-8)

Automatic differentiation provides an alternative to difference formulas for the calculation of derivative data. Neither symbolic algebra nor numerical differencing, derivatives are computed, essentially, by algorithmic application of the chain rule to a reduced (optimized) representation of the operation sequence. Several implementations are available and the approach has been successfully tested on a variety of problems in engineering and operations research. Data presented in Table 4 was produced with the package ADOL-C [10] using double precision (53 significand bits, 15-17 decimal digits). The partial derivative values computed by automatic differentiation agree with those calculated using the adjoint formula to fourteen decimal digits, as indicated by the underscore beneath the first differing digit. These results are especially interesting because no formula for second derivative data is required, merely a slightly modified version of the routine which evaluates the expression for $g(\cdot)$. In our tests, a 16.4 Kbyte temporary storage buffer was required by the ADOL-C package for the partial derivative calculation. This appears to be the primary disadvantage to automatic differentiation: The storage requirements for the derivative calculations can be quite substantial, even for relatively simple functions.

A general-purpose package for numerical pathfollowing of equilibria typically contains a facility for computing the augmented Jacobian using finite-differencing. Here the usual caveats concerning numerical differentiation apply. Finite difference approximation is unreliable, especially applied to functions where accumulated roundoff error is large. High-order formulae require multiple function evaluations. The difference stepsize must be chosen to properly balance the effects of roundoff and truncation error. Table 4 shows a compilation of the partial derivatives, $\frac{\partial}{\partial v} det\,(2\mathbf{J} \odot \mathbf{I}_n)$ and $\frac{\partial}{\partial m} det\,(2\mathbf{J} \odot \mathbf{I}_n)$, computed using both forward (FD) and central (CD) difference formulae for the selected Hopf point. Next to each entry (in parenthesis) is the exponent of the stepsize h which produces the numerical derivative closest to that computed by automatic differentiation. The computed error from stepsize choices substantially larger than h are due to truncation error; stepsizes significantly smaller exhibit roundoff error and, finally, catastrophic cancellation.

3.2. A Model of a Bursting Neuron. The second example we study is a dynamical system used to describe the electrical activity of the Anterior Burster (AB)

neuron in the stomatogastric ganglion of the lobster *Panulirus interruptus*. Based on work of Plant [19] and Rinzel and Lee [20], the model is similar in structure to the Hodgkin-Huxley equations, but more complex. Under certain physiological conditions the AB cell produces complicated, rhythmic patterns of action potentials. Guckenheimer, et al. [12] have shown that some of this behavior is well-described by a 6-dimensional system of ordinary differential equations, referred to in what follows as the RLA (**R**inzel-**L**ee/**A**-current) model for the AB neuron. The model is obtained from that of Rinzel and Lee [20] by a change of time scale and the incorporation of an additional potassium ion current, called the A-current.

Let $x = (x_1, \cdots, x_6) \in \mathbb{R}^6$, denote the vector of independent variables. Components of this vector correspond to the physical model as follows: x_1 is the voltage difference across the cell membrane; x_2 is a dimensionless quantity describing the activity of intracellular free calcium; x_3 controls the activation of the delayed-rectifier potassium channel; x_4 controls the inactivation of the sodium channel; x_5 controls the activation of the calcium channel; x_6 controls the inactivation of the A-current channel. It is convenient to define the model in terms of exponential functions that we denote by:

$$\phi_{\pm}(x_1; \alpha, \beta) \stackrel{\text{def}}{=} \left(1 \pm e^{\alpha+\beta x_1}\right)^{-1}$$

The vector field describing the electrical state of the semipermeable membrane is then given by:

$$\begin{aligned}
\dot{x}_1 &= -g_{Na}\varphi_2^3(x_1)\, x_4\, (x_1 - v_{na}) - 2g_{Ca}x_5\frac{(x_1 - v_{ca})}{(1+2x_2)} - g_K x_3^4\,(x_1 - v_k) - \\
&\qquad 2g_{KCa}x_2\frac{(x_1 - v_k)}{(1+2x_2)} - g_A\psi_2^3(x_1)\, x_6\,(x_1 - v_k) - g_l\,(x_1 - v_l) \\
\dot{x}_2 &= -0.003\left[x_2 - k_{ca}x_5\frac{(x_1 - v_{ca})}{(1+2x_2)}\right] \\
\dot{x}_3 &= 0.8\left[(1 - x_3)\,\varphi_3(x_1) - x_3\psi_3(x_1)\right] \\
\dot{x}_4 &= 0.8\left[(1 - x_4)\,\varphi_4(x_1) - x_4\psi_4(x_1)\right] \\
\dot{x}_5 &= -.042553\left[x_1 - \phi_+(x_1; \alpha_5, \beta_5)\right] \\
\dot{x}_6 &= \phi_+(x_1; \gamma_5, \delta_5) - x_6
\end{aligned}$$

where,

$$\begin{aligned}
\varphi_1(x_1) &= -(\alpha_1 + \beta_1 x_1)\,\phi_-(x_1; \alpha_1, \beta_1) & \psi_1(x_1) &= 4e^{\gamma_1+\delta_1 x_1} \\
\varphi_2(x_1) &= \frac{\varphi_1(x_1)}{\left(\varphi_1(x_1) + \psi_1(x_1)\right)} & \psi_2(x_1) &= \phi_+(x_1; \gamma_2, \delta_2) \\
\varphi_3(x_1) &= -0.1\,(\alpha_3 + \beta_3 x_1)\,\phi_-(x_1; \alpha_3, \beta_3) & \psi_3(x_1) &= 0.125e^{\gamma_3+\delta_3 x_1} \\
\varphi_4(x_1) &= 0.07e^{\alpha_4+\beta_4 x_1} & \psi_4(x_1) &= \phi_+(x_1; \gamma_4, \delta_4)
\end{aligned}$$

The constants which enter these expressions through the functions $\phi_{\pm}$ were matched with the observed rates of activation and inactivation of ion channels in voltage-clamp experiments from other biological systems. Table 5 displays the values used in the numerical tests presented here. In addition, the model contains eleven physiological parameters which describe the various channel conductances and ion-reversal potentials. For our purposes, all parameters but (g_{KCa}, g_A) remain fixed at the nominal values shown in Table 5.

TABLE 5
Experimentally derived constants used in the AB cell model equations.

Subscript	α	β	γ	δ
1	-2.8714	-0.12095	-2.9841	-0.06196
2	–	–	-0.46154	-0.46154
3	-2.3714	-0.12095	-0.42143	-0.015119
4	-2.6857	-0.060476	-2.3714	-0.12095
5	-7.5	-0.15	10.333	0.16667

g_{Na}	15.0 μS	v_{na}	30.0 mV	g_{ca}	0.04 μS
g_A	8.0 μS	v_k	-75.0 mV	g_l	0.0854 μS
k_{ca}	0.0078 mV^{-1}	v_{ca}	140.0 mV	v_l	-40.0 mV

Numerical experiments for the RLA example were performed using a simple predictor/corrector algorithm implemented in the MATLAB© computation environment. Given an initial point at (or near) a solution, a sequence of points is advanced along the Hopf curve in a two-phase process: First, an Euler predictor step is taken using tangent data computed at a previous solution. Then a series of Newton corrector steps is used to return the computed point on the bifurcation set. The length of the step taken between two successive solutions is determined by an algorithm of Georg [7], which seeks to maintain the initial rate of progress (contraction of the objective function values) exhibited by the sequence of corrector steps at a prescribed constant. The program design is very similar to that described by Allgower and Georg [1], suitably adapted for the current problem and MATLAB implementation. To avoid the problems inherent in following Hopf curves which have turning points, we use pseudo-arclength continuation throughout. Using the notation introduced in Equation (4), if $y = (x, g_{KCa}, g_A)$ is the vector of independent variables parameterized by τ, $y(\tau_i)$ is the i^{th} Hopf solution point, $h = \tau_{i+1} - \tau_i$ is the desired steplength and g is one of the defining equations shown in Table 2, then numerical continuation was performed using the augmented system,

$$F(x, g_{KCa}, g_A; \tau) = \begin{pmatrix} f(x, g_{KCa}, g_A) \\ g(x, g_{KCa}, g_A) \\ v^t(\tau_i) \cdot [y(\tau) - y(\tau_i)] - h \end{pmatrix}$$

where $v(\tau_i)$ is the (fixed) unit tangent vector computed at the i^{th} solution.

Figure 1 shows the Hopf bifurcation curve computed using the Bezout resultant, $g = det(\mathcal{B})$, as the augmenting equation. Eight points have been selected and enumerated for comparative purposes. The first labeled point is the initial condition used to start the continuation algorithm, chosen very near the Takens-Bogdanov point which terminates the branch. Points four and six are turning points in the Hopf solution curve with respect to the parameter g_{KCa}, and point five marks a self-crossing of the Hopf branch that gives rise to a double-Hopf bifurcation point. The insert provides a more detailed plot of the region near this degenerate point. Table 6 displays the

phase space coordinates of the selected points while Table 7 shows the parameter space coordinates of each selected point together with the magnitudes of the real and imaginary components of the critical eigenvalues.

TABLE 6
Phase space coordinate data for each selected point shown in Figure 1.

Pt	x_1	x_2	x_3	x_4	x_5	x_6
1	-57.51974	0.25087	0.02357	0.93874	0.24452	0.32154
2	-56.95448	0.26247	0.02506	0.93262	0.26054	0.30134
3	-55.88832	0.28476	0.02810	0.91951	0.29251	0.26530
4	-53.51959	0.33524	0.03610	0.88184	0.37100	0.19570
5	-35.18183	0.57398	0.19477	0.23292	0.90227	0.01132
6	-34.47902	0.57615	0.20525	0.21286	0.91118	0.01008
7	-35.15696	0.57406	0.19513	0.23218	0.90260	0.01128
8	-34.95203	0.57473	0.19816	0.22620	0.90527	0.01090

TABLE 7
Parameter space coordinates (g_{KCa}, g_A) for each selected point shown in Figure 1. Also shown are the magnitudes of the imaginary parts for the critical eigenvalues.

Pt	g_{KCa}	g_A	$\lvert Re(\lambda)\rvert$	$\lvert Im(\lambda)\rvert$
1	-0.114740	5.207732	$<10^{-13}$	0.00125
2	0.154625	3.416376	$<10^{-13}$	0.00694
3	0.373380	1.753603	$<10^{-14}$	0.00942
4	0.468639	0.552728	$<10^{-14}$	0.01049
5	0.248306	1.797327	$<10^{-11}$ $<10^{-4}$	0.01241 0.06766
6	0.235546	2.269719	$<10^{-7}$	0.02252
7	0.270302	0.949501	$<10^{-11}$	0.10536
8	0.286695	2.805522	$<10^{-11}$	0.12937

The loop associated with the double point labeled five in the computed Hopf curve is a bit paradoxical. At the double point, there are two pairs of pure imaginary eigenvalues and continuation around the loop must transform one of these pairs into the other. The mechanism for this transformation involves the geometry of how eigenvalues and eigenvectors depend upon matrices. The set of real $n \times n$ matrices with simple eigenvalues is not simply connected. When following a homotopically nontrivial loop in this set, eigenvalues of a matrix may be permuted. Such an interchange happens in this example. There is a point in the (g_{KCa}, g_A) plane inside the loop of the Hopf curve at which the system has a complex pair of double eigenvalues.

Our numerical experiments using the Bezout augmenting equation with the RLA model indicate that the numerical computation of the coefficients for the Jacobian characteristic polynomial $p(\lambda) = \sum_{k=0}^{5} c_k \lambda^k$ using reduction from the Hessenberg to Frobenius form by simple elimination [26] is reliable and accurate. To explore this observation further, we make the following ansatz: Since the form of the RLA equations permit the explicit symbolic computation of the coefficients $\{c_k\}_0^5$ as functions of the Jacobian entries, we presume that these expressions, evaluated in extended floating point arithmetic at an equilibrium point, are exact. Moreover, we assume that the

eigenvalues and eigenvectors computed using the unsymmetric QR algorithm are exact as well. Using these data we may evaluate how well conditioned the Hopf continuation task is both as an eigenvalue problem and, separately, as a polynomial rootfinding problem. The condition of the eigenproblem is equivalent to the sensitivity of the spectrum of the Jacobian to small perturbations of its elements, $(\mathbf{J} + \epsilon\mathbf{E})$, reflected in the spectral condition number

$$s(\lambda) = \frac{y^H \cdot x}{||y||_2 ||x||_2}$$

where y and x are left and right eigenvectors of $\mathbf{J}$, respectively, of the eigenvalue λ. We expect that, for ϵ small, the perturbation of the eigenvalues will be less than $\delta\lambda = \epsilon||\mathbf{B}||_2/s(\lambda)$ and we consider the eigenproblem well-conditioned if $s(\lambda)$ is near one. The first column of Table 8 presents the spectral condition number for the critical eigenvalues of the Jacobian at each selected point solution. Clearly, the data show that methods based on explicit determination of the spectrum (JGR) or their sums (BP) directly from the Jacobian entries should be relatively insensitive to small perturbations to the elements of $\mathbf{J}$.

TABLE 8

Condition numbers (κ_2) for the Jacobian ($\mathbf{J} = D_x f$), the corresponding companion matrix, and the spectral condition number, s_λ, associated with the pure imaginary eigenvalues.

Pt	s_λ	$\kappa_2(D_x f)$	$\kappa_2(\mathcal{C})$
1	1.0×10^{-2}	2.8×10^{6}	5.8×10^{8}
2	1.7×10^{-2}	2.5×10^{5}	1.7×10^{7}
3	1.5×10^{-2}	2.1×10^{5}	8.6×10^{6}
4	1.4×10^{-2}	1.9×10^{5}	6.8×10^{6}
5	2.0×10^{-3} 4.1×10^{-3}	6.4×10^{6}	2.4×10^{7}
6	9.0×10^{-4}	2.9×10^{7}	2.9×10^{7}
7	9.0×10^{-3}	1.6×10^{6}	9.7×10^{6}
8	1.2×10^{-2}	4.8×10^{5}	6.2×10^{6}

Table 8 also shows 2-norm condition estimates for the Jacobian matrix and its associated companion matrix as computed by Algorithm 1 at the selected points; in each case the reduction results in an inflation of the condition number, but the increase is mild (at most three orders of magnitude). Thus, the main source of instability in the computation of the characteristic polynomial coefficients – the use of non-unitary similarity transformations in the reduction of the Hessenberg form – is well-behaved along the branch of Hopf points. We examine further the classical error estimates of the eigenvalues to the perturbation problem $(\mathcal{C} + \epsilon\mathbf{E})$ where $\mathcal{C}$ is the companion matrix associated with $\mathbf{J}$ and $\mathbf{E}$ is the matrix that contains a single nonzero entry in its n^{th} column (which we take to be one). Now suppose λ_i is a simple root of the characteristic polynomial $charpoly(\mathcal{C}) = p(\lambda) = charpoly(\mathbf{J})$ for $1 \le i \le n$. A small perturbation in the k^{th} coefficient of p,

$$p(\lambda) + \epsilon\lambda^k = \lambda^6 + (c_k + \epsilon)\,\lambda^k + \sum_{i\neq k} c_i\lambda^i$$

may be related to the resulting perturbed root by the linear estimate,

$$\lambda_i + \delta \approx \lambda_i - \epsilon \frac{\lambda_i^k}{\prod_{j \neq i} (\lambda_i - \lambda_j)} \quad .$$

Thus, the relative sensitivity of each *simple* eigenvalue of $\mathbf{J}$ (equivalently, each simple root of p), to small perturbations in the coefficients of the characteristic polynomial are estimated by the magnitudes of the n factors, s_k, given by

$$s_k(\lambda_i) \triangleq \left| \frac{\lambda_i^k}{\prod_{j \neq i} (\lambda_i - \lambda_j)} \right| \quad .$$

The first three columns of Table 9 show, for each selected point, the subscript (k), value (c_k) and factor (s_k) for the coefficient of p upon which the critical eigenvalue is most sensitively dependent. For example, in the case of the last (8^{th}) point, a perturbation of 1% in the value of c_4 will produce a change of approximately 0.5% in the computed critical eigenvalue. These data support the conclusion that relatively small errors in the numerically computed values of the characteristic polynomial coefficients produce only mild perturbations in the roots of p, or equivalently, the computed eigenvalues of $\mathbf{J}$. Thus, construction of the residual polynomials in the first method of Kubiček (K1) may be expected to be well-behaved.

TABLE 9

Characteristic polynomial coefficients of maximal sensitivity for each selected point shown in Figure 1. Data is shown for each of three problems: $p(\lambda)=0$, $r_e(z)=0$ and $r_o(z)=0$ where $z=\lambda^2$.

	$p(\lambda)$			$r_e(z)$			$r_o(z)$		
Pt	k	c_k	$s_k(\lambda)$	k	c_k	$s_k(\lambda)$	k	c_k	$s_k(\lambda)$
1	2	7.0e-3	8.9e-2	2	7.0e-3	2.2e-4	3	1.4e-1	2.5e-5
2	2	6.8e-3	5.1e-1	2	6.8e-3	7.1e-3	3	1.3e-1	7.3e-4
3	2	6.5e-3	7.2e-1	2	6.5e-3	1.4e-2	3	1.2e-1	1.3e-3
4	2	5.9e-3	9.0e-1	2	5.9e-3	1.9e-2	3	1.1e-1	1.6e-3
5	2	7.4e-4	8.9 43.7	2	7.4e-4	2.2e-1 6.8	3	6.0e-3	3.5e-2 1.0
6	2	2.2e-4	53.6	2	2.2e-4	4.2	1	-3.5e-6	163.6
7	1	3.8e-5	676.5	4	1.9e-1	6.9e-2	3	1.7e-2	1.3
8	4	1.9e-1	3.3e-1	4	1.9e-1	1.1e-1	3	1.2	2.1e-2

From Section 2.1, the resultant methods are based on a specific rootfinding problem; that is, to find $z = \lambda^2$ which simultaneously satisfies

$$\left\{ \begin{array}{c} r_e(z) \\ r_o(z) \end{array} \right\} = \left\{ \begin{array}{r} z^3 + c_4 z^2 + c_2 z + c_0 \\ c_5 z^2 + c_3 z + c_1 \end{array} \right\} = \mathbf{0} \quad .$$

Thus, sensitivity of the shared root to perturbations in the coefficients of the two separate polynomials is of interest, and the sensitivity estimates computed above for p may be extended as well to the polynomial pair (r_e, r_o) associated with p. The last

six columns of Table 9 display, for each selected point, the values of s_k for the shared root corresponding to the coefficient of maximal sensitivity.

It is usual, in the discussion of Hopf pathfollowing using direct methods, to assume that a solution $(x^*, \alpha^*; \beta^*)$ on a branch is known and then to proceed to describe how subsequent solutions may be computed beginning with data from this point. However, practical experience suggests that frequently the task of finding one (or more) initial points is *by far* the most time-consuming part of a numerical bifurcation study, especially as the dimension of the phase and parameter spaces increases. We present a comparison of the root-finding convergence regions for the augmented systems based on the Bezout resultant (RB) and the iterative eigensubspace method (JGR) for the RLA model. The Bezout resultant is well-defined at any point in the product space $\mathbb{R}^6 \times \mathbb{R}^2$, and all the information required to begin a corrector sequence at (x_0, g^0_{KCa}, g^0_A) may be derived from the linearization of the vector field at that point. This is not the case for the (JGR) system, which requires estimates for a basis $\{v, w\}$ of the eigenspace associated with the pure imaginary eigenvalue $\pm\omega i$, and a vector l not in $span\,\{v, w\}$. The intuitive choice is to use seed values v_0, w_0, ω_0 and l based on the complex elements of $spec(\mathbf{J})$ with the smallest real part. However, this eigenpair may not become critical for nearby values of (g_{KCa}, g_A), and an incorrect choice can bias the starting conditions away from the solution manifold, requiring many Newton steps to compute a solution, if convergence is achieved at all.

We explore this possibility in a small region of the (g_{KCa}, g_A) parameter space to the right of the double Hopf point in Figure 1. Two segments of Hopf bifurcation (referred to as the upper and lower branches in what follows) intersect at the double Hopf point. The RLA vector field has a single equilibrium for each choice of (g_{KCa}, g_A) in this region; moreover, the spectrum of the Jacobian for each such choice contains at least one complex eigenvalue pair. Since the rate at which the two pairs of complex eigenvalues cross the imaginary axis is very different, the intuitive choice is "correct" only in a thin band above the lower Hopf branch. If a Newton corrector is applied to choices for (g_{KCa}, g_A) in this parameter region, the results reflect the underlying structure in the spectrum of the equilibria, as shown in Figure 2. The lower plot shows data collected using the augmented system, (JGR). A 75×75 point grid was established over the 2-parameter regime. For each point in the grid, the unique equilibrium was found and the complete spectrum was computed. The complex eigenpair closest to the imaginary axis was used to compute starting values for the augmented variables and Newton's method was used to solve the nonlinear systems with $g(\cdot)$ chosen as in the (JGR) system of Table 2. The convergence criterion used was $||\mathbf{D}F||_\infty < TOL$, where $\mathbf{D}$ was a *constant* diagonal scaling matrix chosen to equilibrate the disparate magnitudes of the various components in the objective function. If convergence was not achieved within 30 Newton steps, the trial was considered a failure. Successful trials are labeled with a triangle if they converged to the upper branch, a circle if to the lower branch. Thus, the plot shows the ultimate fate of a choice (g_{KCa}, g_A) given perfect information for the Jacobian at the starting conditions.

As expected, the set of converged initial conditions divides the parameter grid into roughly two parts, those which converge to the upper branch and those to the lower branch. Below the lower branch, the Jacobian has one complex eigenpair and computing the initial augmented variables based on the spectrum at the gridpoint is usually successful. In between, the dividing line occurs along the locus of intersection for the real parts of the two eigenpairs. Since this locus occurs very close to the lower branch, a disproportionate fraction of successful trials starting near the lower branch

leave the neighborhood of the nearest Hopf bifurcations, U. Instead of correcting the errant starting conditions for v_0, w_0, ω_0, the Newton sequence "corrects" the phase and parameter coordinates. In this example, computing v_0, w_0, ω_0 for starting conditions very near the lower branch using the "wrong" eigenpair still frequently results in a converged solution. In the general case, there is no reason why the delusive eigenpair need cross the imaginary axis at all; indeed, such a situation would typically be expected to result in convergence failure.

The analogous experiment was performed using the Bezout resultant, $g = det(\mathcal{B})$; the results are displayed in the upper plot of Figure 2. Again, the parameter region is divided by points which converge to the upper and lower Hopf branches. In this case, however, the distribution is more even. In particular, the lower branch exhibits a robust convergence neighborhood. A band of initial conditions which do not result in successful Newton sequences appears between the two Hopf branches, a zone outside the region of local convergence for Newton's method for any point in Γ. Such a failure zone is expected for any choice of augmenting functions, and occurs where the quadratic model for the objective function, F, ceases to be sufficient to ensure adequate descent. A natural algorithmic improvement is to employ globally convergent variants of Newton's method to improve the behavior far from the solution set. In this context, a properly-constructed quasi-Newton method must involve two steps: First, the full Newton step must be computed, and appropriate criteria for sufficient decrease in F evaluated. If the Newton step results in satisfactory progress, the full step is taken; otherwise, a modified step is computed. A common criterion is to guarantee that the result of the candidate step be a (sizable) fraction of the predicted improvement based on the gradient of F at the current point. More precisely, if y_k is the k^{th} step of a corrector sequence and δy is the Newton step, then the algorithm accepts the full step if

$$F(y_k + \delta y) < F(y_k) + \epsilon[\nabla F(y_k)]^t \delta y \tag{15}$$

for some $0 < \epsilon < 1$. Typically, ϵ is chosen quite small, but it is significant that the obvious selection $\epsilon = 0$ is insufficient to ensure global convergence; some positive improvement in the objective function is required.

Figure 3 shows the result of applying the criterion (15) to the convergence experiment described above. At each step in the corrector sequence, the acceptance criterion was evaluated with $\epsilon = 0$; the point was deemed a failure if the inequality was not satisfied. Points which survive as successful trials not only converged to a Hopf bifurcation point, but also made monotonic progress toward the solution at each corrector step. Thus, if a steplength adjustment (e.g., line search or dogleg) algorithm were used to improve global convergence behavior based on the acceptance criteria above (for $\alpha = 0$), the full Newton step would be accepted at each step. The results for the augmented function $g = det(\mathcal{B})$ indicate that points near the border of the non-convergence zone of Figure 2 are characterized by Newton steps which, early in the corrector sequence, do not strictly improve the objective function. However, apart from this band, most initial conditions are within the local convergence neighborhood. For the (JGR) augmenting function, nearly 50% of the trials which converge to a Hopf point without the monotonicity condition are *rejected* according to step acceptance criteria. This may be compared to a 23% reduction for the resultant method.

We regard the questions of accuracy and convergence considered above as more important than the speed of algorithms that detect Hopf detection in examples of moderate size. Nonetheless, we present some brief comparative data for our implementations of three algorithms within Matlab©. For each of the Bezout resultant,

biproduct matrix and JGR methods from Table 2, we computed 20 points along a Hopf bifurcation curve shown in Figure 1 starting at a point along the curve and proceeding with an identical continuation algorithm. The floating point operation counts were comparable for the Bezout (664777 flops) and JGR methods (701244 flops) while the biproduct calculation was substantially slower (2786163 flops). Note, however, that the biproduct calculations did not exploit the sparsity of the biproduct matrix in computing its determinant. The biproduct method seems to offer the best opportunity to exploit the calculation of low dimensional invariant subspaces in high dimensional problems.

3.3. A Larger Neural Model. Based on extensive experimental results, Golowasch [8] proposed a fourteen-dimensional system of ordinary differential equations as a model for the LP neuron in the stomatogastric ganglion of the crab, *Cancer borealis*, that incorporates the effects of eight separate ionic currents. The parameters which govern the activation kinetics for the associated conductance channels were derived from space-clamped experimental data. Buchholtz [4] later amended this model; our third example is a twelve-dimensional variation of these equations.
Despite the complexity of this system, analytic Jacobian derivatives were derived using Maple©. Using,

$$\begin{aligned}\psi(u,v,\alpha) &= e^{\frac{(u-v)}{\alpha}} \\ \phi\left(u,v,\alpha\right) &= \left(1+\psi(u,v,\alpha)\right)^{-1} \quad .\end{aligned}$$

the model equations for the LP neuron are given by:

$$\begin{aligned}
\dot{x}_1 &= -c_{10}(g_{ca1}x_9x_{11} + g_{ca2}x_{10})(x_2 - \varphi_4(x_1)) + c_{20}(c_8 - x_1) \\
\dot{x}_2 &= (c_1 - ((g_{ca1}x_9x_{11} + g_{ca2}x_{10})(x_2 - \varphi_4(x_1)) + g_l(x_2 - e_l) + \\
&\quad g_d x_4^4(x_2 - e_k) + g_{KCa}x_5x_6(x_2 - e_k) + g_a x_8 x_7^3(x_2 - e_k) + \\
&\quad g_h x_{12}(x_2 - e_h) - c_{11}(\tfrac{1}{2}c_2(\varphi_5(x_2,x_3) - \varphi_6(x_2,x_3)))))/c_{11} \\
\dot{x}_3 &= k_h\left[c_6(1-x_3)\psi(x_2,c_{44},c_{27}) - x_3\phi(x_2,c_{50},c_{33})\right] \\
\dot{x}_4 &= c_{12}\phi(x_2,c_{52},c_{35})\left((\phi(x_2,c_{54},c_{37}) - x_4\right) \\
\dot{x}_5 &= k_{oa}(\varphi_7(x_1,x_2) - x_5) \\
\dot{x}_6 &= c_{21}\left(\frac{c_4}{(c_5+x_1)} - x_6\right) \\
\dot{x}_7 &= c_{16}(\phi(x_2,c_{41},c_{24}) - x_7) \\
\dot{x}_8 &= c_{15}(\phi(x_2,c_{48},c_{31}) - x_8) \\
\dot{x}_9 &= c_{17}(\phi(x_2,c_{42},c_{25}) - x_9) \\
\dot{x}_{10} &= c_{18}(\phi(x_2,c_{43},c_{26}) - x_{10}) \\
\dot{x}_{11} &= c_{19}(\phi(x_2,c_{49},c_{32}) - x_{11}) \\
\dot{x}_{12} &= \frac{c_{13}(\phi(x_2,v_r,c_{38}) - x_{12})}{\phi(x_2,c_{53},c_{36})}
\end{aligned}$$

$$\begin{aligned}
\varphi_1(x_2) &= \frac{c_7(x_2 - c_{45})}{1 - \psi(x_2,c_{45},c_{28})} \\
\varphi_2(x_2) &= \frac{\varphi_1(x_2)}{\varphi_1(x_1) + c_8\psi(x_1,c_{50},c_{33})}
\end{aligned}$$

$$\varphi_3(x_1) = \log\left[\psi(x_1, \tfrac{1}{100}, \tfrac{3}{100}) + \psi(x_1, -\tfrac{1}{100}, -\tfrac{3}{100})\right]$$

$$\varphi_4(x_1) = c_{56} - c_{57}\ \log\left[\tfrac{2}{300}\varphi_4(x_1) + \tfrac{1}{3}(100x_1 - 1) + \tfrac{1}{100}\right]$$

$$\varphi_5(x_2, x_3) = \frac{1}{c_2}\left(\frac{g_{Na}x_3\varphi_2^3(x_2)(e_{na} - x_2)}{c_{11}} - c_1\right)$$

$$\varphi_6(x_2, x_3) = \log\left(e^{\varphi_5(x_2,x_3)} + e^{-\varphi_5(x_2,x_3)}\right)$$

$$\varphi_7(x_1, x_2) = \frac{x_1}{(c_3 + x_1)}\phi(x_2, c_{46} - c_{14}x_1, c_{29})\phi(x_2, c_{47} - c_{14}x_1, c_{30})$$

Table 10 lists the nominal values and units of the parameters.

TABLE 10
Values for the experimentally-determined constants appearing in the LP model equations.

c_1	60000	c_{16}	142.857	c_{31}	6	c_{46}	0	e_l	-50
c_2	6000	c_{17}	50	c_{32}	8	c_{47}	16	g_d	0.35
c_3	2.5	c_{18}	10	c_{33}	-5	c_{48}	-70	g_{KCa}	3.2
c_4	0.7	c_{19}	16	c_{34}	-13	c_{49}	-50	g_a	1.7
c_5	0.65	c_{20}	360	c_{35}	-22	c_{50}	-40	g_{Ca1}	0.21
c_6	0.08	c_{21}	35	c_{36}	-13	c_{51}	-34	g_{Ca2}	0.047
c_7	0.11	c_{22}	166.6	c_{37}	-17	c_{52}	10	g_h	0.037
c_8	0.05	c_{23}	-12	c_{38}	7	c_{53}	-110	g_{Na}	2300
c_9	15	c_{24}	-26	c_{39}	15	c_{54}	-25	g_l	0.1
c_{10}	300	c_{25}	-7	c_{40}	-40	c_{55}	-7	k_{oa}	1
c_{11}	0.0017	c_{26}	-7	c_{41}	-12	c_{56}	115.47	k_h	600
c_{12}	180	c_{27}	-8	c_{42}	-11	c_{57}	12.19	v_r	500
c_{13}	0.33	c_{28}	-20	c_{43}	22	I	0	e_k	-80
c_{14}	0.6	c_{29}	-23	c_{44}	-39	e_h	-10		
c_{15}	20	c_{30}	-5	c_{45}	-6	e_{na}	50		

The LP equations illustrate a difficulty that arises in using the determinant as an indicator of matrix singularity for methods based on polynomial resultants or biproducts. Bounds imposed by the magnitude of $det(\mathcal{B})$ or $2\mathbf{J}\odot\mathbf{I}$ on numerical continuation and failures that arise as a result of (implicitly) treating $det(\cdot)$ as a matrix condition number. These remarks pertain, not only to the use of $det(\mathcal{B})$ or $2\mathbf{J}\odot\mathbf{I}$ in Hopf path following, but also other applications which use the determinant as an objective function in root finding or optimization (detection of saddle-node bifurcations, for example). Thus, progress in addressing these issues in the context of Hopf continuation has implications to other applications, and vice versa.

The bifurcation diagram of the LP equations in the (I_{ext}, g_{Na}) plane has a fold in the surface of equilibrium points that produces a curve of saddle-node bifurcations. A cusp occurs along the fold, dividing the saddle-node bifurcation set into upper and lower branch segments. Along the upper branch, one of the fixed points annihilated in the saddle-node interaction undergoes a change of stability, producing a curve of Hopf points proximal to the saddle-node curve. The Hopf branch arises at a Takens-Bogdanov point and leaves the parameter regime of physiological interest.

Table 11 shows parameter coordinates for four selected points along the Hopf branch described above. Also listed are values for the phase space variables and the complete spectrum. Notice that the critical eigenvalues begin with zero magnitude but

become the eigenvalues of largest magnitude at point four along the branch of Hopf bifurcations and that there are several additional eigenvalues of large magnitude.

TABLE 11

Phase space and parameter coordinates for three selected points along the Hopf curve for the LP equation. Also shown is the complete spectrum for each selected point.

	1	2	3	4
I_{ext}	-0.2099885	0.089912	5.557706	5.496061
g_{Na}	2268.22	1678.89	525.271	3347.40
x_1	0.146623	0.162821	0.196959	0.400147
x_2	-42.979	-39.121	-13.076429	3.657527
x_3	0.270205	0.129938	0.003136	0.000387
x_4	0.257771	0.303509	0.668495	0.843663
x_5	$3.41 \cdot 10^{-5}$	$9.383 \cdot 10^{-5}$	0.017156	0.073446
x_6	0.878709	0.861198	0.826486	0.666574
x_7	0.232991	0.260550	0.489651	0.646162
x_8	0.010949	0.005786	$7.581 \cdot 10^{-5}$	$4.66 \cdot 10^{-6}$
x_9	0.010268	0.017684	0.426381	0.890031
x_{10}	$9.30 \cdot 10^{-5}$	0.000161	0.006621	0.067840
x_{11}	0.293669	0.204259	0.009801	0.001221
x_{12}	$2.90 \cdot 10^{-4}$	0.000167	$4.05 \cdot 10^{-6}$	$3.71 \cdot 10^{-7}$
λ_1	-599.58	-598.88	-569.96	$10^{-8} + 936.86i$
λ_2	-375.99	-377.33	-369.14	$10^{-8} - 936.86i$
λ_3	-152.47	-203.60	$10^{-9} + 278.76i$	-586.36
λ_4	-137.87	-141.86	$10^{-9} + 278.76i$	-383.02
λ_5	-62.76	-60.72	-143.02	-142.86
λ_6	-35.09	-35.23	-131.49	-90.53
λ_7	-20.26	-20.10	-48.64	-50.28
λ_8	-15.47	-16.57	-32.69	-36.86
λ_9	-9.95	-9.95	-20.00	-20.00
λ_{10}	-2.09	$10^{-5} + 8.99i$	-13.73	-15.93
λ_{11}	$10^{-4} + 0.01i$	$10^{-5} - 8.99i$	-11.01	-11.13
λ_{12}	$10^{-4} + 0.01i$	-0.33	-0.33	-0.33

One difficulty is immediately apparent from these data: If $\lambda_i = \bar{\lambda}_{i+1}$ is the critical eigenpair and the remaining real eigenvalues are arranged in descending order, $\lambda_j \geq \lambda_{j+1}$ for $j \neq i, i+1$, then to achieve a prescribed solution tolerance $||F(x^*, I^*_{ext}, g^*_{Na})||_\infty < \epsilon$ requires

$$Re(\lambda_i) < \frac{\epsilon}{2} \left[\prod_{\substack{k=3 \\ k \neq i, i+1}}^{12} \lambda_k^{k-3} \left(\lambda_k^2 + |\lambda_i| \right) \right]^{-1}$$

using the rough estimate that $(\lambda_i + \lambda_j) \approx max(\lambda_i, \lambda_j)$ for eigenvalue pairs that do not approach zero in a neighborhood of a solution. For large systems, or even small systems with a few large eigenvalues, this explosion in the magnitude of the biproduct determinant or resultant severely restricts the size of the neighborhood about the

solution manifold where the computed value contains any significant digits. In the LP equations, the effect is prohibitive.

To apply the algebraic Hopf methods previously described to problems of this type requires a strategy for eliminating the disabling effects of the unwanted large eigenvalues, so long as they do not participate in the bifurcation. One possible approach involves substituting an alternative method for determining when $2\mathbf{J} \odot \mathbf{I}_n$ or $det(\mathcal{B})$ is singular. For example, if a true condition estimate was substituted for $det(\cdot)$, such as

$$g(x, I_{ext}, g_{Na}) = || \left(2\mathbf{J} \odot \mathbf{I}_n\right)^{-1} ||_F^{-1} \tag{16}$$

where $|| \cdot ||_F$ is the Frobenius norm, the required differentiability properties are retained. Another alternative, suggested by Allgower, et al. [2] in the context of using multi-dimensional resultants to compute real polynomial roots, is the function:

$$g(x, I_{ext}, g_{Na}) = \min_{||u||=1} || \left[2\mathbf{J} \odot \mathbf{I}_n\right] u||_2^2 \ . \tag{17}$$

Notice that this is equivalent to iteratively driving the smallest singular value σ_n to zero and, thus, uses the square of the 2-norm condition number as the augmenting equation. This choice is especially attractive since σ_n is widely considered the most reliable estimate of matrix condition, and several different methods for its computation might be adapted to the problem of Hopf pathfollowing. In the continuation framework it may also be possible to make use of spectral information computed at wide intervals and updated cheaply at intermediate solution points. For example, suppose that at (or near) a solution $(x^0, I_{ext}^0, g_{Na}^0)$, the full set of eigenvalues $\lambda_1, \cdots, \lambda_n$ and corresponding eigenvectors $v_1, \cdots, v_n$ are computed. Then, by the elementary properties of the biproduct matrix, a vector in the nullspace of $\mathbf{J} \odot \mathbf{I}_n$ can be formed: Using the lexicographic ordering scheme introduced in Section 2.3, if v_p^i is used to denote the i^{th} component of the p^{th} eigenvector, we can construct an eigenvector, V, corresponding to the eigenvalue $\lambda_i + \lambda_j$ of $2\mathbf{J} \odot I_n$ according to the formula:

$$V_{\{ij\}}^{\{pq\}} = det \begin{bmatrix} v_i^p & v_j^p \\ v_i^q & v_j^q \end{bmatrix} \tag{18}$$

where $1 \leq j, p \leq n-1$ and $2 \leq i, q \leq n$. This vector may be stored and used to start a conjugate gradient algorithm (for example), constrained to the unit sphere, as an estimate for u in Equation (17) to compute subsequent corrector steps. (See [2] for a discussion of the conjugate gradient method applicable to this situation).

An important special case arises when some of the large eigenvalues are associated with an invariant subspace which evolves slowly as the parameters are varied. More precisely, suppose at a point $(x^0, I_{ext}^0, g_{Na}^0)$ near a Hopf bifurcation the range of the (non-singular) Jacobian matrix $\mathbf{J}_0$ may be split into a direct sum of eigenspaces $W_c \oplus W_h$, with $dim(W_c) = m$ and $dim(W_h) = n - m$, such that:

1. Locally, W_h contains the 2-dimensional subspace corresponding to the Hopf bifurcation;
2. W_c contains some of the large eigenvalues in the spectrum of $\mathbf{J}_0$, and
3. W_c remains nearly invariant as $\mathbf{J}$ is perturbed away from $\mathbf{J}_0$.

Then we may eliminate the unwanted effects of W_c altogether by deflating the Jacobian to form a new matrix that has only the eigenvalues associated with W_h. The literature on matrix deflation in the context of eigenvalue determination is vast;

explicit techniques are central to iterative methods and implicit use of deflation is integral to various Lanczos schemes. In our preliminary experiments we used a simple algorithm based on similarity transformations. Suppose an $n \times m$ rectangular matrix $\mathbf{U}$ can be obtained with linearly independent columns so that $range(\mathbf{U}) = W_c$. Then applying Gaussian elimination we form the product, $\mathbf{\Sigma}$, of elementary matrices that triangularize $\mathbf{U}$:

$$\mathbf{\Sigma U} \equiv \mathbf{QPU} = \begin{bmatrix} \mathbf{T} \\ - - - \\ \mathbf{0} \end{bmatrix}$$

where $\mathbf{T}$ is upper triangular and reference to the permutation matrix $\mathbf{P}$ is made explicit to emphasize the use of partial pivoting to stabilize the transformation. Applying $\mathbf{QP}$ to $\mathbf{J}$ produces a block-structured equation involving the Jacobian:

$$\mathbf{\Sigma J} = \begin{bmatrix} \mathbf{J}_{11} & \mathbf{J}_{12} \\ \mathbf{E} & \mathbf{J}_{22} \end{bmatrix} \mathbf{\Sigma}$$

where $\mathbf{J}_{11}$ is an $m \times m$ matrix. It follows easily that if $\mathbf{U}$ is chosen as above, $\mathbf{U}$ commutes with $\mathbf{J}$ if and only if $\mathbf{E} = \mathbf{0}$ and, if so, $spec\,(\mathbf{J}_{22})$ displays the same set of eigenvalues as does $\mathbf{J}$ on W_h (See Wilkinson [27, Chapter 9, Sections 21-24] for a discussion).

Given a candidate splitting $W_c \oplus W_h$, the sensitivity of the deflating subspace $range(\mathbf{U})$ to perturbations in the Jacobian matrix is properly expressed in terms of the *separation* of the matrices $\mathbf{J}_{11}$ and $\mathbf{J}_{22}$, measured by:

$$sep\,(\mathbf{J}_{11}, \mathbf{J}_{22}) = \min_{\mathbf{X} \neq \mathbf{0}} \frac{||\mathbf{J}_{11}\mathbf{X} - \mathbf{X}\mathbf{J}_{22}||}{||\mathbf{X}||}$$

where $\mathbf{X}$ ranges over the subspace of $p \times (n-p)$ matrices. The $sep(\cdot,\cdot)$ function is difficult to compute, in general, but bounds exist based on the spectra of the matrix arguments (when $\mathbf{J}$ is diagonalizable):

$$\begin{aligned} s_l\,(\mathbf{J}_{11}, \mathbf{J}_{22}) &= \frac{\min |spec(\mathbf{J}_{11}) - spec(\mathbf{J}_{22})|}{\kappa_2\,(\mathbf{Q}_1)\,\kappa_2\,(\mathbf{Q}_2)} \\ &\leq sep\,(\mathbf{J}_{11}, \mathbf{J}_{22}) \\ &\leq \min |spec(\mathbf{J}_{11}) - spec(\mathbf{J}_{22})| = s_u\,(\mathbf{J}_{11}, \mathbf{J}_{22}) \end{aligned}$$

where $\mathbf{Q}_1$ and $\mathbf{Q}_2$ are chosen to diagonalize $\mathbf{J}_{11}$ and $\mathbf{J}_{22}$, respectively. Equality holds on the right when $\mathbf{J}$ is normal but, in general, the separation of $\mathbf{J}_{11}$ and $\mathbf{J}_{22}$ may be much less than the minimum distance between the respective spectra. Procedures for the numerical estimation of $sep(\cdot,\cdot)$ have been proposed [5], similar in form to well-known methods of matrix condition estimation. Table 12 shows values for $s_l(\cdot,\cdot)$, $sep(\cdot,\cdot)$ and $s_u(\cdot,\cdot)$ for six choices of W_c of increasing dimension, m, for the LP model Jacobian. Each case corresponds to a choice for W_c that contains the m-largest real eigenvalues of $\mathbf{J}$ evaluated at the second point of Table 11.

A simple strategy for incorporating deflation of the Jacobian into numerical Hopf pathfollowing is the following: Suppose the complete eigenstructure for $\mathbf{J}$ is computed at the initial solution point on the Hopf branch (by any method), m is determined by $sep()$ estimates and the columns of $\mathbf{U}$ are chosen to be the appropriate eigenvectors

TABLE 12

Separation function values and bounds for deflations of dimension 2 to 7 for the LP model equations. Each p-dimensional deflating subspace contains the p-largest real eigenvalues of the Jacobian matrix at the initial branch point.

p	$s_u()$	$sep()$	$s_l()$
2	174	36	2
3	62	3	$6{\cdot}10^{-2}$
4	81	7.0	$8{\cdot}10^{-2}$
5	26	2.5	$2{\cdot}10^{-2}$
6	15	$4{\cdot}10^{-1}$	$2{\cdot}10^{-3}$
7	4	$3{\cdot}10^{-1}$	$4{\cdot}10^{-4}$

of $\mathbf{J}$. At each subsequent corrector step $||\mathbf{E}||_F$ is computed and, if sufficiently large, the columns of $\mathbf{U}$ are updated using a small number of inverse iteration steps. Notice that each column may be adjusted independently, so if $m >> (n-m)$ and n is of moderate size, this step can be performed in parallel. Numerical continuation was begun at selected point 2 of Table 11 using g_{Na} as the continuation parameter, and proceeded toward the Takens-Bogdanov point at the beginning of the branch (near point 1). The 7-dimensional deflating subspace of Table 12 was used and updated at each corrector step. The residual real part of the critical eigenpair is below 10^{-12} near the beginning of the curve and remains below 10^{-9} as the solutions approach the Takens-Bogdanov bifurcation.

4. Concluding Remarks. We have examined the application of minimal augmentation methods for computing Hopf bifurcations to three examples of vector fields that describe the electrical activity of axons and neurons. There are several conclusions we draw from this work.

1. The derivation of symbolic expressions for the detection of Hopf bifurcations in families of vector fields of moderate complexity is feasible. The usefulness of these symbolic expressions is dependent upon the complexity of expressions for the Jacobian of a vector field and upon the effectiveness of root finding algorithms.

2. Automatic differentiation algorithms work. They give far more accurate values for derivatives than are obtainable with the simplest finite difference methods of computing derivatives.

3. Continuation applied to minimal augmentation methods for finding Hopf bifurcations appear to work at the singularities associated with double Hopf bifurcations in two parameter families of vector fields. The root finding problem has a singularity of corank 1 at these points, but the method appears to follow the smooth branches of solutions passing through this point with little difficulty. This success calls for further theoretical justification.

4. In at least some circumstances, the minimal augmentation methods are preferable to direct methods that require the computation of eigenvectors. In the example we present, iterative root finding algorithms that start with natural choices for their initial seeds converge more reliably and have larger regions of convergence for the minimal augmentation methods than for the direct methods that solve for eigenvectors.

5. In problems that are large or stiff, straightforward implementation of the minimal augmentation methods lead to root finding problems that are poorly conditioned. The difficulty lies in the determination of when a large matrix with eigenvalues of large

magnitude is singular. By using the extensive numerical linear algebra theories for calculating the condition number of a matrix, the algorithms for detecting Hopf bifurcations can be significantly improved. Implementations based on calculations of the smallest singular value of a matrix appear to be an attractive target for further work in this area.

6. Despite the growth in the size of the linear algebra problems that are associated with the definition of the biproduct matrix as a strategy for computing Hopf bifurcations, the impact of this growth can be ameliorated by the intelligent use of standard algorithms for linear algebra problems. These increase the sparsity of the biproducts whose condition number must be calculated or localize these calculations to smaller matrices calculated from the biproduct.

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Figure 1: Curve of Hopf bifurcation points in the two-parameter plane (g_{KCa}, g_A) for the RLA neuron model computed using the Bezout resultant augmenting function (RB). Eight selected points corresponding to the entries in Table 6 are distinguished along the curve. The segment of the solution curve shown in the insert has been transformed by a simple rotation to make the closed loop visible at these scales.

Figure 2: Convergence data for Newton's method in a neighborhood of Hopf branches in the (g_{KCa}, g_A) parameter plane. The upper plot shows data for the Bezout resultant (RB) as the augmented function; the lower plot shows data for the method of Jepson/Griewank/Reddien (JGR). Triangle symbols show initial condition which ultimately converge to the upper Hopf branch while circles indicate convergence to a lower branch point.

Figure 3: Convergence data for Newton's method in a neighborhood of Hopf branches in the (g_{KCa}, g_A) parameter plane including a monotonicity condition on the sequence of corrector steps. The upper plot shows data for the Bezout resultant (RB) as the augmented function; the lower plot shows data for the method of Jepson/Griewank/Reddien (JGR). Triangle symbols show initial condition which ultimately converge to the upper Hopf branch while circles indicate convergence to a lower branch point.