THE ROLE OF HOMOTOPY TECHNIQUES IN BIOMEDICAL MODELLING: A CASE STUDY

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Abstract

Homotopy methods are not rare in the computational analysis of parametrized nonlinear systems of equations and the corresponding nonlinear physical phenomena these equations represent. The numerical analyst can use homotopies as a device to lead to convergence to a solution of an otherwise insoluble problem. Also, some physical systems depend on a natural parameter, and we use homotopy or continuation methods to study the behavior of the system as this parameter varies. However, the modeller can also employ similar techniques to efficiently generate a family of solutions in cases where one or more parameters in the model are both unknown and not unambiguously calculable from the data.

In this paper, we introduce the basic mathematical framework and raison d'etre for homotopy methods, and we mention other applications where they have been appropriate and successful. We then indicate how such methods could be used in dipole models and other models of the sources of cerebral evoked potentials.

1. Introduction and Basic Ideas

Mathematically, a homotopy is a system of equations of the form

$$\begin{aligned} h_1(x_1, x_2, \ldots, x_n, \lambda) &= 0 \\ h_2(x_1, x_2, \ldots, x_n, \lambda) &= 0 \\ &\vdots \\ h_n(x_1, x_2, \ldots, x_n, \lambda) &= 0 \end{aligned} \qquad (1)$$

where λ is the homotopy parameter. Such systems can arise either as mathematical constructions or from natural physical situations. For example, the h_i could represent a discretization of the equations of fluid dynamics, and λ could represent velocity or Reynolds number. Alternately (if $n = 3$), the h_i could represent the position on a screen of the intersection of surfaces in space, and λ could represent a viewing angle.

It is sometimes convenient to think of λ as an undistinguished argument x_{n+1}. Then, using matrix notation, (1) becomes

$$\begin{aligned} &H(X) = 0, \quad \text{where} \\ &H(X) = (h_1(X), h_2(X), \ldots, h_n(X))^T, \quad \text{and} \\ &X = (x_1, \ldots, x_{n+1})^T, \end{aligned} \qquad (2)$$

where the superscript "T" indicates that we think of H and X as column vectors. If we know an X_0 such that $H(X_0) = 0$, then additional solutions (for alternate parameters λ) may be computed by solving the differential-algebraic system

$$\begin{aligned} &J(X)\,X' = 0, \qquad X(0) = X_0, \\ &R(X') = 1, \end{aligned} \qquad (3)$$

where J is the n by $n+1$ Jacobian matrix of H and where R is some normalization function (such as $\|X'\|_2$).

Computational methods based on equation (3) are termed continuation methods. Their execution is often reliable and efficient, compared to solving (1) with differing values of λ as a set of unrelated problems. Reviews of continuation methods appear in (1), (3), and (7). Software package descriptions are found in (9), (16), (7), and elsewhere. These methods make homotopy techniques (i.e., formulation and solution of systems of the form (1)) practical.

In Section 2, to illustrate the place of homotopies in scientific computing, we mention additional non-biomedical applications of homotopy techniques; we then briefly explain the context in which we may use homotopies. In Section 3, we give some details on how these techniques might be applied to models of the sources of cerebral evoked potentials. Implementation details and numerical results will appear elsewhere.

2. Illustrative Applications

Homotopy methods can be used as a mathematical device to compute all solutions to a system of nonlinear equations or to compute solutions at which Newton's method or other methods diverge. A simple H for this purpose is the following Garcia/Zangwill homotopy.

$$H(X) = x_{n+1}F(x_1, \ldots, x_n) + (1 - x_{n+1})G(x_1, \ldots, x_n). \qquad (4)$$

Here, F represents the system of nonlinear equations we wish to solve, and G represents a (simpler) system of equations for which solutions $(\bar{x}_1, \ldots, \bar{x}_n)$ are known. Solving $F = 0$ can thus be done by following the solution to (3) from $x_0 = (\bar{x}_1, \ldots, \bar{x}_n, 0)$ to $X = (x_1, \ldots, x_n, 1)$.

The theory and practical aspects of this idea are well-developed in the context of finding all solutions to polynomial systems of equations. They are explained in (7). In (15), etc., (4) and other homotopies are applied to more general problems which are directly linked to applications. An interesting such application is also given in (2). Application to nonlinear least squares problems is discussed in (5) and (10).

A notable employment of continuation methods to study behavior of naturally parametrized systems is to fluid mechanics problems; a discussion of this appears in (6). Also, application of the methods to CAD/CAM graphics is discussed in (8). In fact, such applications are ubiquitous, especially in biological modelling, and underly the study of stability, bifurcation, and chaos.

Here, we propose a slightly different use. We do not construct an artificial homotopy merely to solve a nonlinear system, nor do we solve (3) in order to study the behavior of a physical system as a parameter changes. Instead, we begin with parametrized models, and we wish to compute the parameters from the data. Such fitted parameters, though mathematically correct, may, due to ill-conditioning, etc., be physically unmeaningful. In our technique, we fix one of the parameters, then compute the family of fits with respect to the other parameters as we vary the fixed one. Human observation of the way these fits change then leads to insight into the actual physical situation.

3. Homotopies for Evoked Potential Dipole Models

Two models of multiple or extended sources of evoked potential responses may benefit from a homotopy approach. The first is appropriate, for example, to model simultaneous bilateral median nerve stimulation. We assume the source consists of two current dipoles, given by position vectors p_1 and p_2 and moment vectors m_1 and m_2. In our standard procedure, we measure voltages V_i at points A_i on the scalp, for $1 \leq i \leq m$, with m usually between 6 and 36. Letting $V(p, m; A_i)$ be the voltage at point A_i due to a dipole at position p and with moment vector m, we then compute the 12 parameters representing the components of p_1, m_1, p_2, and m_2 by minimizing the function

$$\psi(p_1, m_1, p_2, m_2) = \sum_{i=1}^{m} \{V_i - [V(p_1, m_1; A_i) + V(p_2, m_2; A_i)]\}^2. \quad (5)$$

Though we have successfully used (5) for simulated bilateral median nerve stimulation, the model is not always well-posed. For example, any two dipoles whose positions and moments satisfy $p_1 = p_2$ and $m_1 = -m_2$ fit the zero potential field perfectly. We intuitively expect such cancellation and resultant ambiguity to also occur in cases in which the optimal positions are close, and possibly in other cases as well. In the presence of noisy data, such ambiguity could lead to parameter fits which are difficult to interpret physically.

As an alternative to (5), we may introduce a homotopy parameter λ, and we minimize ψ_2 defined by

$$\psi_2(p_1, m_1, p_2, m_2) = \psi(p_1, m_1, p_2, m_2) + \lambda(\|m_1\|_2^2 + \|m_2\|_2^2) \quad (6)$$

with respect to p_1, p_2, m_1, and m_2. When the second term on the right in (6) is small, there can be less cancellation in the moment vectors. Thus, a large value of λ will result in less cancellation in the fit. On the other hand, a small value of λ will result in a closer fit to the actual data. We propose to compute a number of two-dipole fits as we vary λ. We then use our judgment to infer properties of the actual source.

The second model is appropriate when there is thought to be a diffuse electrically active surface (cf. (14), (12), and (13)). We assume a source in the form of a spherical cap of electrically active dipoles with angular extent w at radius r from the origin, and with moment density m. (See Figure 1.)

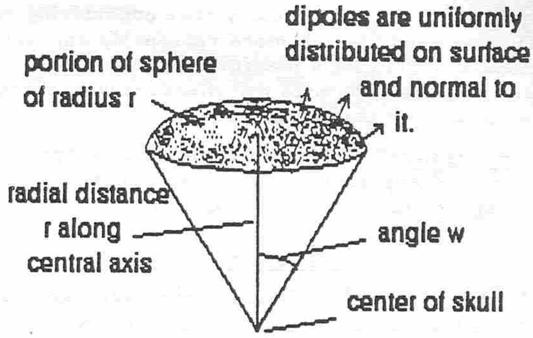

Figure 1. A spherical cap of dipoles.

Additional parameters include ϕ and θ, which are the angles (in the usual spherical coordinate system) describing the direction of the central axis of the cap. Let $V(r, w, m, \phi, \theta; A_i)$ denote the voltage at point A_i due to such a spherical cap. We may attempt to determine all five parameters in such a cap by minimizing

$$\psi_c(r, w, m, \phi, \theta) = \sum_{i=1}^{m} \{V_i - V(r, w, m, \phi, \theta; A_i\}^2. \quad (7)$$

(In practice, we replace the parameter m by an "intensity," which is m divided by the area of the cap surface.)

We have obtained mathematically unambiguous values of r, w, m, ϕ, and θ when fitting the P-300 compoment of certain 28-lead data from auditory stimulation, where the fit represented a wide yet centric source (i.e., the algorithm robustly determined a large w and r near zero). However, it is unclear whether such fits are always a reasonable approximation to the actual electrically active surface. Also, we have met with less success on other data sets.

One problem with ψ_c is that caps with small r ("centric" caps), small w, and large m give similar voltage distributions to caps with r nearer to 1 ("superficial" caps), large w, and smaller m (cf. (11)). To resolve this ambiguity, we may think of either r or w to be a fixed "homotopy" parameter. We then fit with respect to the other parameters. For example, if we select r to be the homotopy parameters, we obtain a series of plausible caps, from centric ones to superficial ones. We then use our judgment to infer properties of the actual source.

It is tempting to apply a homotopy method to the imaging technique described in (4). There, we compute an approximate potential distribution on the cortical surface, given data at the scalp leads A_i. This technique involves computing parameters on a test surface which is different from the cortical surface. The accuracy of the potential function on the cortical surface depends on the location of the test surface, and the optimal location is not known *a priori*. We could thus use the radius of the test surface as a homotopy parameter. However, the system to be solved in this technique is linear.

Because of this, there would be no advantage of using continuation method machinery over considering each problem as separate. A more reasonable approach would be to formulate a measure of the accuracy of the answer, then optimize that measure with respect to the location of the test surface.

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References

(1) E. Allgower and K. Georg, "Simplicial and continuation methods for approximating fixed points and solutions to systems of equations," SIAM Rev. Vol. 22, No. 1, pp. 28-85, Jan., 1980.

(2) G.D. Byrne and L.A. Baird, "Distillation calculations using a locally parametrized continuation method," Computers and Chemical Engineering, Vol. 9, No. 6, pp. 593-599, 1985.

(3) C.B. Garcia and W.I. Zangwill, Pathways to Solutions, Fixed Points, and Equilibria. Englewook Cliffs, N.J.: Prentice-Hall, 1981.

(4) C.D. Hill, R.B. Kearfott, and R.D. Sidman, "The inverse problem of electroencephalography using the singular value decomposition," these proceedings.

(5) R.B. Kearfott, "Continuation methods and parametrized nonlinear least squares: techniques and experiments" in Numerical Methods, V. Pereyra and A. Reinoza, eds., Lecture Notes in Mathematics, No. 1005, Springer Verlag, Berlin, 1983, pp. 142-151.

(6) H.B. Keller, "Continuation methods in computational fluid dynamics," in Numerical and Physical Aspects of Aerodynamic Flows, T. Cebeci, ed., Springer Verlag, Berlin, 1982, pp. 3-13.

(7) A.P. Morgan, Solving Polynomial Systems Using Continuation for Engineering and Scientific Problems. Englewood Cliffs, N.J.: Prentice-Hall, 1987.

(8) A.P. Morgan, "The continuation method," General Motors Research Laboratories Report No. GMR-5723, (submitted to Computer Graphics in the Arts and Sciences), 1987.

(9) W.C. Rheinboldt and J.V. Burkardt, "A locally parametrized continuation process," ACM Trans. Math. Software, Vol. 9, No. 2, pp. 215-235, June, 1983.

(10) D.E. Salane, "A continuation method for solving large-residual nonlinear least squares problems," SIAM J. Sci. Statist. Comput., Vol. 8, No. 4, pp. 655-671, July, 1987.

(11) R.D. Sidman and R.B. Kearfott, "The inverse problem of electroencephalography assuming double layer neural generators," these proceedings.

(12) R.D. Sidman and D.B. Smith, "Localization of the neural generators of scalp-recorded potentials by means of mathematical models," in Modelling of Biomedical Systems, J. Eisenfeld and M. Whitten, eds., Elsevier Science Publishers, Amsterdam, 1986, pp. 205-211.

(13) R.D. Sidman, D.B. Smith, J.S. Henke, R.B. Kearfott, and V. Giambalvo, "The use of equivalent source models in evoked potential research and differential diagnosis," in Frontiers of Engineering in Health Care, A.R. Potvin and J.H. Potvin, eds., IEEE, 1986, pp. 205-211.

(14) H.G. Vaughan, Jr., "Analysis of scalp-recorded brain potentials," Bioelectric Recording Techniques: Part B, Electroencephalography and Human Brain Potentials, B.F. Thompson and M.M. Patterson, eds., New York: Academic Press, 1974.

(15) L.T. Watson, "Engineering applications of the Chow-Yorke algorithm," in Homotopy Methods and Global Convergence, B.C. Eaves, F.J. Gould, H.-O. Peitgen, and M.J. Todd, eds., New York and London: Plenum, 1983.

(16) L.T. Watson, S.C. Billups and A.P. Morgan, "HOMPACK: A suite of codes for globally convergent homotopy algorithms," ACM Trans. Math. Software, Vol. 13, No. 3, pp. 281-310, September, 1987.