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COMMUNICATIONS

^{31}P NMR Bayesian Spectral Analysis of Rat Brain *in Vivo*

G. LARRY BRETTHORST, JOHN J. KOTYK, AND JOSEPH J. H. ACKERMAN

Department of Chemistry, Washington University, St. Louis, Missouri 63130

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Bayesian spectrum analysis for parameter estimation is a rigorous statistical (non-Fourier-based) method. Herein the Bayesian quadrature NMR model is introduced and applied to analysis of ^{31}P NMR time domain data from *in vivo* rat brain. Immunity to both the brain spectrum "baseline hump" and the phase twist is demonstrated.

INTRODUCTION

We recently introduced the use of Bayesian spectral analysis and parameter estimation (*1–3*) for application to classical high-resolution NMR time domain free induction decay data (*4*). As a rigorous statistical (non-Fourier-based) method, Bayesian analysis makes use of available prior information to optimize parameter estimates for an assumed model function while eliminating (integrating out) "nuisance parameters" from the estimation/optimization procedure. In this communication, we introduce the Bayesian quadrature NMR model, which utilizes prior information regarding the $\pi/2$ phase shift between data channels, and demonstrate the robust nature of this method via analysis of *in vivo* ^{31}P NMR rat brain data. Specifically, we demonstrate analysis immunity to both the brain spectrum "baseline hump" and the phase twist.

BAYESIAN QUADRATURE NMR MODEL

Consider data (D) sampled at discrete times (t_i) and stored in real [$d_R(t_i)$] and imaginary [$d_I(t_i)$] quadrature channels of the form

$$d_R(t_i) = f_R(t_i) + n(\sigma, 0) \qquad \text{and} \qquad d_I(t_i) = f_I(t_i) + n(\sigma, 0), \qquad [1]$$

where $n(\sigma, 0)$ is a Gaussian noise component of mean zero and and standard deviation σ, $f_R(t)$ is the model of the signal in the real channel, and $f_I(t)$ is the model for the imaginary channel. We write these model signals as

$$f_R(t) = \sum_{j=1}^{m} B_j G_j(t) \qquad \text{and} \qquad f_I(t) = \sum_{j=1}^{m} B_j F_j(t). \qquad [2]$$

The signal functions $G_j(t)$ and $F_j(t)$ are functions of a continuous variable t sampled at discrete times $t_i = \{t_1, \ldots, t_N\}$, not necessarily uniform. Typically, the signal

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functions are functions of other continuous parameters. For example, in the case of a single decaying sinusoid, the signal function could be written

$$f_R(t) = (B_1 \cos \omega t + B_2 \sin \omega t)e^{-\alpha t} \quad \text{and} \quad f_I(t) = (B_1 \sin \omega t - B_2 \cos \omega t)e^{-\alpha t}. \quad [3]$$

The two nonlinear parameters to be estimated are the frequency, ω, and the decay rate, α. We will label all of these nonlinear parameters collectively as $\{\theta\}$ with the understanding that they could be frequencies, decay rates, or any other nonlinear parameters needed to model the signal.

Although the amplitudes $\{B\}$ (and phase information therein) are of interest, Bayesian probability theory (*1–3*) allows formulation of the optimum estimation (posterior probability) of the nonlinear frequencies and decay rates, $\{\theta\}$, independently of the amplitude $\{B\}$ and the noise variance σ^2. Note that quadrature information has been incorporated into the model by assuming that the amplitudes $\{B\}$ are the same in both channels.

A detailed derivation of the posterior probability is beyond the scope of this communication and will be submitted at a later date. However, it can be shown that the posterior probability of the frequencies and decay rates conditional on the data (D) and prior information (I) is given as

$$P(\{\theta\} \mid D, I) \propto \lambda_1^{-1/2} \cdots \lambda_m^{-1/2} \left[1 - \frac{m\overline{h^2}}{d_R \cdot d_R + d_I \cdot d_I} \right]^{(m-2N)/2}, \quad [4]$$

where the following definitions apply,

$$\overline{h^2} \equiv \frac{1}{m} \sum_{k=1}^{m} h_k^2, \quad [5]$$

$$h_k = R_k \cdot d_R + I_k \cdot d_I, \quad [6]$$

$$R_k = \sum_{j=1}^{m} \frac{G_j e_{kj}}{\sqrt{\lambda_k}}, \quad [7a]$$

$$I_k = \sum_{j=1}^{m} \frac{F_j e_{kj}}{\sqrt{\lambda_k}}, \quad [7b]$$

where e_{jk} is the kth component of the jth eigenvalue of the interaction matrix

$$g_{jk} \equiv G_j \cdot G_k + F_j \cdot F_k \quad [8]$$

and λ_j is its jth eigenvalue and $(\cdot)$ means sum over discrete times. For example,

$$G_j \cdot G_k \equiv \sum_{i=1}^{N} G_j(t_i) G_k(t_i). \quad [9]$$

The expected amplitudes $\langle B_k \rangle$ are easily computed from the maximum posterior probability. If we define $\{\hat{\theta}\} = \{\hat{\theta}_1, \ldots, \hat{\theta}_n\}$ as the values that maximize Eq. [4], then the amplitudes $\langle B_k \rangle$ are given by

$$\langle B_k \rangle = \sum_{j=1}^{m} \frac{h_j e_{jk}}{\sqrt{\lambda_j}} \bigg|_{\{\hat{\theta}\}}. \quad [10]$$

Explicit estimates of the precision of the amplitudes $\{B\}$ and the nonlinear $\{\hat{\theta}\}$ parameter are easily derived, but that derivation is also beyond the scope of this communication. See Ref. (*2*) for an example of this procedure.

The Bayesian analysis gives a simple intuitive picture of quadrature model fitting; the data may be considered to be in a $2N$-dimensional linear vector space, and the model may be considered an m-dimensional subspace. The frequencies and decay rates which maximize the posterior probability, Eq. [4], are those which allow the model to make the closest approach to the data by the mean square criterion.

APPLICATION TO *IN VIVO* SPECTROSCOPY

^{31}P NMR data were acquired at 145.8 MHz (8.5 T) using a standard single-coil surface-coil antenna (*5*) placed on the head of an anesthetized (halothane) male Spraque–Dawley rat (ca. 250 g). Rapid repetition pulse-and-collect acquisition was employed with a pulse width of 15 μs at 100 W, 2K complex data points, a 15,151-Hz bandwidth, and a pulse repetition period of 87 ms; 501 free induction decays (FID) were summed to memory.

A segment of the ^{31}P time domain data set covering 3 to 17 ms is shown in Fig. 1A. The early portion of this segment shows strong evidence of multicomponent damped sinusoidal decay. The very early portion of the complete FID (not shown) contained evidence of a large-amplitude rapidly decaying signal(s). The same segment of the model is shown in Fig. 1B. The model contains eight nonstationary frequencies and displays a high level of agreement with the experimental data. This is emphasized in Fig. 1C, which shows the residuals, the differences between the model and the experimental data. Note that there is some structure remaining at early time points in the residual plot, suggesting additional frequency components not accounted for in the eight-component model. These components could be readily extracted if they were of interest.

Although the Bayesian analysis provides estimates of the relevant NMR observables directly, for illustrative purposes the Fourier transforms of the entire experimental and model FIDs are given in Fig. 2. Fourier transformation of the experimental data (Fig. 2A) shows the expected pattern of primary resonances from ATP, phosphocreatine, inorganic phosphate, and phosphomonoesters (*5, 6*). These relatively narrow resonances are superimposed on the familiar brain ^{31}P "baseline hump" arising from bone and membrane phospholipid head groups (*7, 8*). The transform of the model FID yields essentially the same absorption spectrum, but without noise. Both experimental and model absorption spectra contain a strong first-order (in frequency) phase twist, *vida infra*.

The presence of phase twists and nonideal baselines are problems that complicate quantitative analysis of spectroscopic and imaging data. These artifacts result from representing time domain data as absorption mode frequency domain spectra. As a parameter estimation procedure, Bayesian analysis easily accounts for such artifacts. This is illustrated in Fig. 2C where the metabolic resonances of interest are displayed free of phase or baseline distortions. This was accomplished by discarding the two very rapidly exponentially decaying components responsible for (upon Fourier transformation) the baseline hump and in using knowledge of individual component phase and amplitude, $\{B\}$, to present a pure absorption frequency domain spectrum.

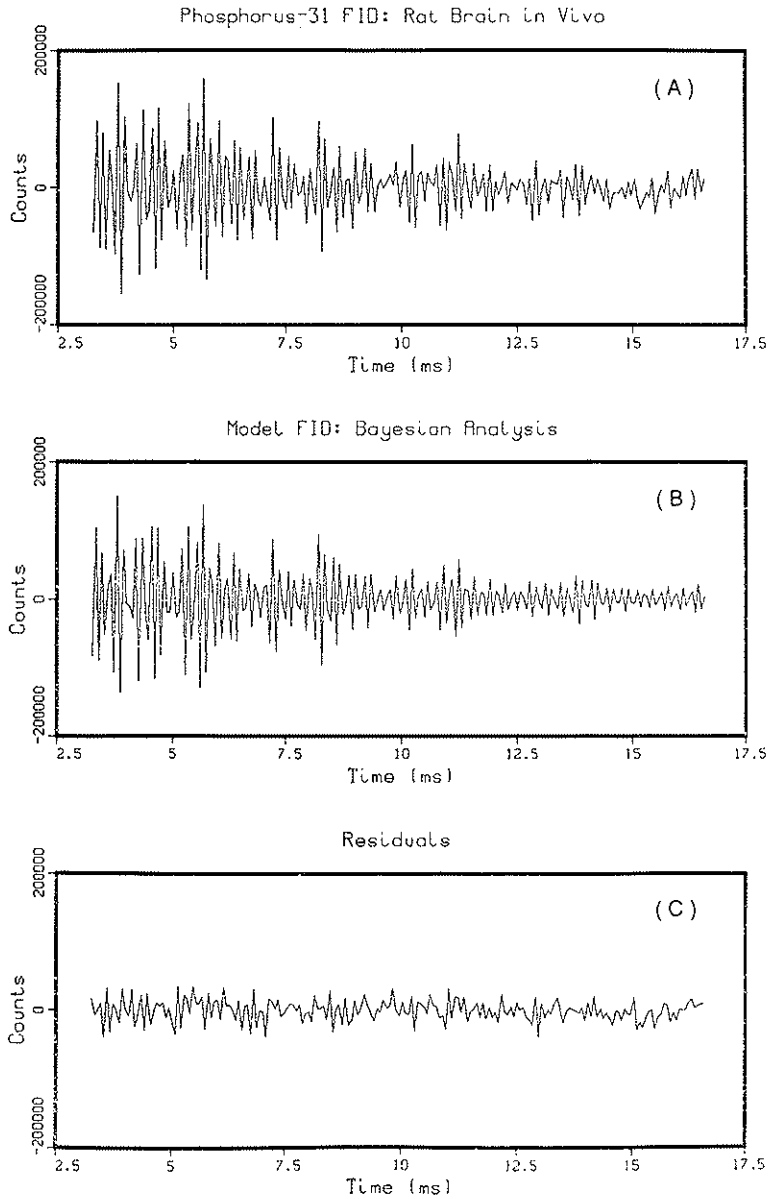

FIG. 1. (A) Segment of experimental time domain data (^{31}P free induction decay) from rat brain *in vivo*. (B) Equivalent segment of eight-component model FID whose parameters were estimated via Bayesian analysis. (C) Equivalent segment of residuals, the difference between the model and the experimental FIDs. Vertical and horizontal scales are equivalent for all three panels.

In summary, the Bayesian quadrature analysis method can be used readily with quadrature data sets obtained on current generation pulsed NMR spectrometers. As in the previous nonquadrature Bayesian NMR analysis method (*4*), optimal parame-

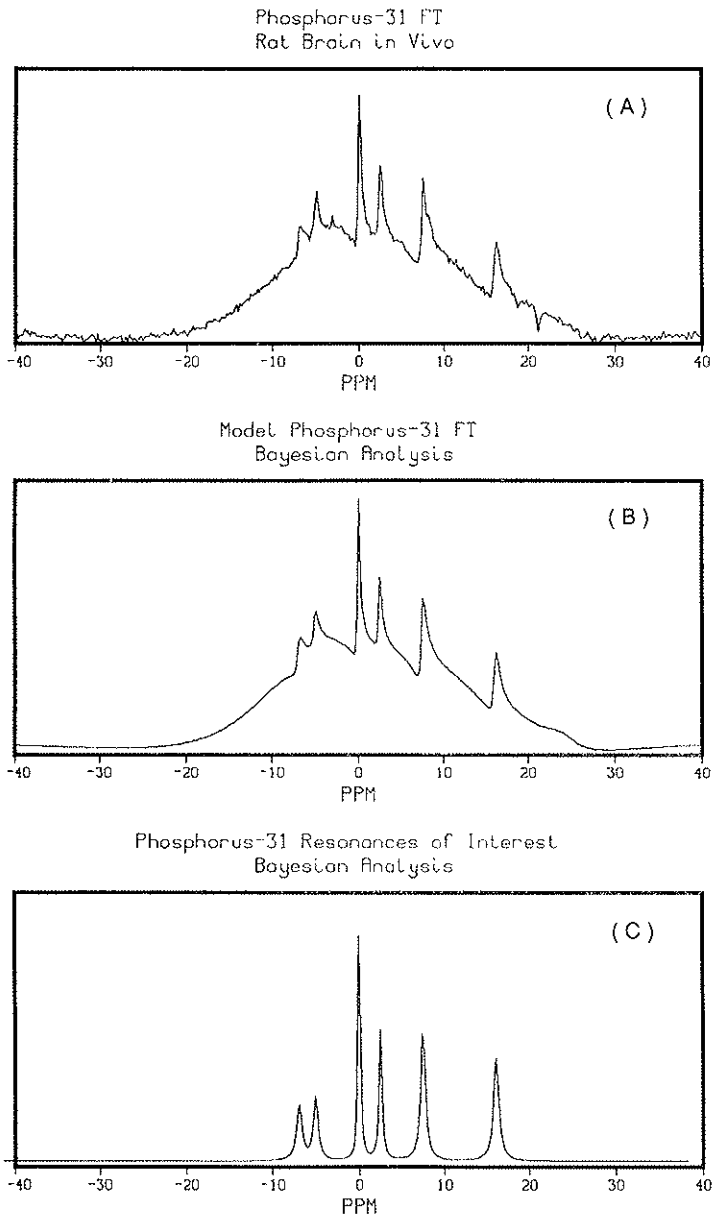

FIG. 2. (A) Fourier transform of the complete experimental ^{31}P FID from rat brain *in vivo*, a segment of which is displayed in Fig. 1A. (B) Fourier transform of the complete eight-component model FID whose parameters were estimated via Bayesian analysis, a partial segment of which is displayed in Fig. 1B. (C) Fourier transform of the model FID after removal of the two rapidly decaying components and setting all remaining component phases to zero.

ter estimates, $\{\theta\}$, are obtained while "nuisance parameters" such as component amplitude and phase, $\{B\}$, are integrated out of the search procedure to be readily recovered later. Because it is a time domain analysis method, frequency domain phase and baseline distortion do not corrupt parameter estimation. While the Bayesian approach is computer intensive relative to Fourier transform (minutes-to-hours vs tenths of seconds-to-seconds), the benefits of such a rigorous statistical approach and the availability of powerful but inexpensive computers make this technique practical.

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