Honoris Causa Celebration

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System Identification and NMR Spectroscopy

Congratulations Alan and David

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Outline of the talk

• What is NMR and and how is it used in the determination of the structure of proteins?

2. What is the mathematical description of the NMR system?

3. What makes the system identification problem hard and how does "2-D" signal processing help?

4. A new theorem that describes the optimal effect that control can have on the identification process via the Cramer-Rao bound associated with system identification.

Why this topic for this occasion?

1. Alan has a long interest in signal processing and control and they are entwined here.

• Alan cut (some of his) teeth on Lie algebraic methods and they play a role here.

3. The material makes contact with a number of areas of scientific inquiry and seems suitable for a broad audience.

4. I like it!

An unfolded alpha helix structure.



Part 1: The Concept of Quantum Mechanical Spin

First postulated as property of the electron for the purpose of explaining aspects of fine structure of spectroscopic lines, (Uhlenbeck-Gouldsmit). Electron spin was first incorporated into a Schrodingerlike description of physics by Pauli and then treated in a definitive way by Dirac. Spin itself is measured in units of angular momentum as is Plank's constant. The gyromagnetic ratio links the angular momentum to an associated magnetic moment which, in turn, accounts for some of the measurable aspects of spin. Protons were discovered to have spin in 1927 (Dennison) and in 1932 Heisenberg wrote a paper on nuclear structure in which the recently discovered neutron was postulated to have spin and a magnetic moment.

In this talk it is the net spin of the **nucleus** that plays the basic role, although there is an important indirect effect (the chemical shift) involving electronic spin also playing a role.

Angular Momentum and Magnetic Moment Spin (angular momentum) relative to a fixed direction in space is quantized. The number of possible quantization levels depends on the total momentum. In the simplest cases (spin one-half systems) the total momentum is such that the spin can be only plus or minus $h/4\pi$. Systems that consist of a collection of n such states give rise to a Hermitean density matrix of dimension 2^n .by 2^{n} .



Wolfgang Pauli

Werner Heisenberg



The Hilbert Space for Spin

The Hilbert space which occurs in quantum mechanics is a space of square integrable functions mapping the set of possible configurations into the complex numbers. For pure spin systems, unlike, say, the quantum description of a harmonic oscillator, the Hilbert space is finite dimensional.



John von Neumann

Paul Dirac



Boltzmann Distribution for a Physical System in Equilibrium at Temperature T

 $\rho(x)=(1/Z)\exp(E(x)/2kT)$

Because magnetic moments that are aligned with the magnetic field have a little less energy than those opposing it, the Boltzmann distribution implies they are favored.





Part II: The Mathematical description of the System



 $dM/dt = BXM + R(M - M_0)$

Bloch constructed and important phenomenological equation, valid in a rotating coordinate system, which applies to a particular type of time varying magnetic field.

Bloch Nuclear Induction

$$dx_{r}/dt = Ax_{r} + b$$

$$A = \begin{bmatrix} -\frac{1}{T_{2}} & \omega - \omega_{0} & 0\\ -\omega + \omega_{0} & -\frac{1}{T_{2}} & \omega_{1}\\ 0 & -\omega_{1} & -\frac{1}{T_{1}} \end{bmatrix}$$



Purcell Absorption

 ω is rf frequency, ω_0 is precession frequency

Possible Input-Output Response



The frequency of the decaying oscillation reveals the strength of the effective magnetic field felt by the spinning nucleus.

The Linearization Dilemma

Small input makes linearization valid but gives small signal-to-noise ratio. Large input give higher signal-to-noise ratio but makes nonlinear analysis necessary.



An input-output description of the system

$$\frac{d}{dt} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} = \begin{bmatrix} -1 & u & 0 \\ -u & -1 & f \\ 0 & -f & -1 \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} + \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix} + \begin{bmatrix} w_1 \\ w_2 \\ w_3 \end{bmatrix}$$
$$y = x_2 + n$$

Let x be the net angular momentum vector. Let w and n be white noise. The spectroscopic problem is to choose u to reduce the uncertainty in f, given the observation y.

Observe that there is a constant bias term. Intuitively speaking, one wants to transfer the bias present in x_1 to generate a bias for the signal x_2 which then shows up in y.

Qualitative Analysis Based on the Mean

If we keep u at zero there is no signal. If we apply a pulse, rotating the equilibrium state from $x_1 = 1$, $x_2=0$, $x_3=0$ to $x_1 = 0$, $x_2=1$, $x_3=0$, Then we get a signal that reveals the size of f. The actual signal with noise present can be expected to have similar behavior.



Controlling an Ensemble with a Single Control

The actual problem involves many copies with almost the same dynamics

 $dx_1/dt = A(u)x_1 + Bw_1$

 $dx_2/dt = A(u)x_2 + Bw_2$

.

 $dx_n/dt = A(u)x_n + Bw_n$

 $y = (cx_1 + cx_{2+} \dots + x_n) + n$

The system is not controllable or observable. There are something like 10^{23} copies of the same, or nearly the same, system. We can write an equation for the sample mean of the x's, for the sample covariance, etc. Multiplicative control is qualitative different from additive.

In a Stationary (Laboratory) Coordinate System

dx/dt = Ax + b

	$-\frac{1}{T_2}$	$-\omega_0$	sin <i>wt</i>	
$\bar{A} =$	ω_0	$-\frac{1}{T_2}$	$\cos \omega t$	
	$-\sin\omega t$	cos Wt	$-\frac{1}{T_1}$	
[_	$\frac{1}{T}$	$-\omega_0$	$u(t)\sin\omega$	t
$\bar{A} = $	\mathcal{D}_{0}	$-\frac{1}{T}$	$u(t)\cos\omega$	t
-u(t))sin <i>wt</i>	$-u(t)\cos^{-u(t)}$	$\omega t = -\frac{1}{T_{\star}}$	

Why are Radio Frequency Pulses Effective

dx/dt = (A+u(t)B)x

Let z be exp(-At)x so that the equation for z takes the form

 $dz/dt = u(t)e^{-At}Be^{At}z(t)$

If Ax(0)=0 and if the frequency of u is matched to the frequency of exp(At) there will be secular terms and the solution for z will be approximated by z(t) = exp(Ft)x(0). Thus x is nearly exp(At)exp(Ft)x(0).

The Meaning of the Density Matrix, Decoherence

Each ψ has a phase angle but only $|\psi|$ is related to probability, Thus for a single particle phase is not detectable. However for two noninteracting particles the relative phase angle matters. The size of the off-diagonals in ρ measures the consistency of the relative phase angles.

Spin (angular momentum) relative to a fixed direction in space is quantized. The number of possible quantization levels depends on the total momentum. In the simplest cases the total momentum is such that the spin can be only plus or minus 1/2. Systems that consist of a collection of such states give rise to a density matrix of dimension 2^n .

The Density Equation from Statistical Mechanics

The density matrix satisfies a linear equation derived from the wave equation. In studying NMR it is almost always simplified by eliminating many of the degrees of freedom. The resulting equation looks more complicated but it is more easily related to measurements.

The Bloch equation might be regarded as an extreme simplification of a reduced equation of this form

$$\frac{d\rho}{dt} = [iH, \rho]$$

$$\frac{d\sigma}{dt} = [iH, \sigma] + L(\sigma) + n$$

$$\rho = \begin{bmatrix} \rho_{11} & \rho_{12} \\ \rho_{21} & \rho_{22} \end{bmatrix}$$

$$\sigma = \rho_{11}$$

Part III: Why is the identification problem so hard?



Gespard De Prony

Prony's problem

Suppose we are given $y(t_k) + \kappa n(t_k)$ with the $n(t_k)$ being zero mean Gaussian random variables of unit variance and wish to find (possibly complex) vectors $b = [b_1, b_2, ..., b_n]^T$ and $\lambda = [\lambda_1, \lambda_2, ..., \lambda_n]^T$ such that

$$y(t_k) = \sum_{i=1}^n b_i e^{\lambda_i t_k}$$
; $k = 1, 2, 3, ...$

As suggested by the Cramer-Rao bound, a key role is played by the linear term in the Taylor

The Taylor series gives important insight

series expansion

$$\sum_{i=1}^{n} (b_i + \delta_i) e^{(\lambda_i + \gamma_i)t_k} = \sum_{i=1}^{n} b_i e^{\lambda_i t_k} + \sum_{i=1}^{n} \delta_i e^{\lambda_i t_k} + \sum_{i=1}^{n} b_i \gamma_i t_k e^{\lambda_i t_k} + \dots$$

It is convenient to adopt a vector-matrix notation. Let Λ and b be defined as

$$\Lambda = \begin{bmatrix} \lambda_1 & 0 & \dots & 0 \\ 0 & \lambda_2 & \dots & 0 \\ \dots & \dots & \dots & \dots \\ 0 & 0 & \dots & \lambda_n \end{bmatrix} ; b = \begin{bmatrix} b_1 \\ b_2 \\ \dots \\ b_n \end{bmatrix}$$

and let η denote a row vector whose entries are all ones. Then, in a notation in which the

There is a structured matrix involved

derivative is expressed as a row vector, we have

$$\left[\begin{array}{cc} \frac{\partial \eta e^{\Lambda t} b}{\partial b} & \frac{\partial \eta e^{\Lambda t} b}{\partial \Lambda} \end{array}\right] = \left[\begin{array}{cc} \eta e^{\Lambda t} & t b^T e^{\Lambda t} \end{array}\right]$$

Observe that if the real parts of λ_i and λ_j are negative then for all nonnegative integers k

$$\int_0^\infty t^k e^{\bar{\lambda}_i t} e^{\lambda_j t} dt = \frac{(-1)^{k+1} k!}{(\bar{\lambda}_i + \lambda_j)^{k+1}}$$

so that

$$\int_0^\infty t^k e^{\bar{\Lambda}t} e^{\Lambda t} dt = W_{k+1}(\Lambda)$$

Here it is

with W_k being the Hermitean matrix



Lemma 1: Let η be the row vector [1, 1, ..., 1], let Λ be a diagonal matrix whose diagonal entries have negative real parts, and let b be a column vector with complex entries. Considered as a mapping from (b, λ) to $L_2[0, \infty)$, the

As a Fisher Information matrix

Jacobian of

$$\phi(b,\lambda)(t) = \eta e^{\Lambda t} b$$

is

to

$$J = \begin{bmatrix} \frac{\partial \psi}{\partial b} & \frac{\partial \psi}{\partial \Lambda} \end{bmatrix} = \begin{bmatrix} \eta e^{\Lambda t} & t b^T e^{\Lambda t} \end{bmatrix}$$

The Moore-Penrose inverse of J maps $L_2[0, \infty)$
to \mathbb{C}^{2n} and is given by

$$J^{\#}(\cdot) = F^{-1} \int_{0}^{\infty} \left[\begin{array}{c} e^{\bar{\Lambda}t} \eta^{T} \\ t e^{\bar{\Lambda}t} \bar{b} \end{array} \right] (\cdot) dt$$

where

$$F = \begin{bmatrix} W_1 & W_2 * (\eta^T b^T) \\ W_2 * (\bar{b}\eta) & W_3 * (\bar{b}b^T) \end{bmatrix}$$

It is nonsingular if the eigenvalues are distinct

The matrix F is positive definite if and only if the λ_i are distinct and all the components of bare nonzero.

Remark 1: The matrix F provides a measure of the linear independence of the effects of changing the parameter vectors b and λ and as such might be thought of as an *identifiably Gramian*, akin to the controllability and observability Gramians of linear control theory.

Proof: The derivatives evaluated at (b, Λ) can be identified with the vectors having $L_2[0, \infty)$

...more

components

$$\frac{\partial \psi}{\partial b} = \begin{bmatrix} e^{\lambda_1 t} & e^{\lambda_2 t} & \dots & e^{\lambda_n t} \end{bmatrix} ; \quad \frac{\partial \psi}{\partial \Lambda} = \begin{bmatrix} b_1 t e^{\lambda_1 t} & b_2 t e^{\lambda_2 t} & \dots & b_n t e^{\lambda_n t} \end{bmatrix}$$

Form the 2n-dimensional vector

$$J(t) = \begin{bmatrix} \frac{\partial \psi}{\partial b} & \frac{\partial \psi}{\partial \lambda} \end{bmatrix}$$

and observe that if we regard J as defining a map from \mathbb{C}^{2n} to $L_2[0,\infty)$ then the adjoint is the integral operator

$$J^*(\cdot) = \int_0^\infty J^{\dagger}(t)(\cdot)dt$$

...more

Thus the role of $A^{\dagger}A$ in the Moore-Penrose inverse is played by the matrix

$$F = \int_0^\infty \int_0^\infty \left[\begin{array}{c} e^{\bar{\Lambda}t} \eta^T \\ t e^{\bar{\Lambda}t} \bar{b} \end{array} \right] \left[\begin{array}{c} \eta e^{\Lambda t} & t b^T e^{\Lambda t} \end{array} \right] dt$$

identified in the lemma. The evaluation of Frequires only the properties of W_k established above, together with the observation that $W_1 *$ $(\eta^T \eta) = W_1$ By construction, F is Hermitean and nonnegative definite. It will be positive definite unless there is a linear combination of the

...more

functions

$$\{e^{\lambda_1 t}, e^{\lambda_2 t}, ..., e^{\lambda_n t}, b_1 t e^{\lambda_1 t}, b_2 t e^{\lambda_2 t}, ..., b_n t e^{\lambda_n t}\}$$

that vanishes. It is a familiar fact from the theory of ordinary linear differential equations that these functions are linearly dependent if and only if $\lambda_i = \lambda_j$ for some $i \neq j$, assuming that the b_i are all nonzero.

An Example worth considering

For example, if the Gramian of $\psi(b,\lambda)(t) = b_1 e^{\lambda_1 t} + b_2 e^{\lambda_2 t}$ is evaluated at $\psi(t) = e^{-t} + e^{-2t}$ then F is the four-by-four matrix

$$F = \begin{bmatrix} \frac{1}{2} & \frac{1}{3} & \frac{1}{4} & \frac{1}{9} \\ \frac{1}{3} & \frac{1}{4} & \frac{1}{9} & \frac{1}{16} \\ \frac{1}{3} & \frac{1}{4} & \frac{9}{9} & \frac{1}{16} \\ \frac{1}{4} & \frac{1}{9} & \frac{2}{8} & \frac{2}{27} \\ \frac{1}{9} & \frac{1}{16} & \frac{2}{27} & \frac{2}{64} \end{bmatrix}$$

The eigenvalues of this matrix range from about 5×10^{-5} to about .88. The smallest eigenvalue has an associated eigenvector $v^T \approx [.60, -.58, -.18, -.52]$. If we observe $\dot{y}(t) = b_1 e^{-\lambda_1 t} + b_2 e^{-\lambda_2 t} + \kappa \dot{w}$ on $[0, \infty)$ the rms error in determining $b_1 - b_2 - b_1 e^{-\lambda_1 t} + b_2 e^{-\lambda_2 t}$

... continued

 $.5\lambda_1 - \lambda_2$ is about 244κ for the given values of the parameters. Clearly, even in such an unexceptional situation, reasonable identification of b and λ requires a very small value of κ . Marginalizing the probability distribution for the error by eliminating the dependence on b increases the size of the smallest eigenvalue, reducing the rms error associated with its eignevector to about 33κ . This ill conditioning is consistent with, and even to be expected, given the well documented difficulties with Prony's problem.

The 2-D technique modal mixing for better identification



The 2-D technique modal mixing for better identification

Postponing for now some details, this approach leads to a modified problem of the Prony type, now involving the fitting a function of two variables $y(t,\tau)$ with an exponential approximation. The exponents used in the expansion must be shared so the problem takes the form

$$y(t,\tau) \approx \sum_{i=1,j=1}^{n,n} b_{ij} e^{\lambda_i t} e^{\lambda_j \tau}$$

Moreover, there are constraints on the b_{ij} limiting the number of independent variables to 2nas above. This will become clear in the development below.

The measure of the improvement in the accurcy is reflected in the Fisher information matrix which, as we will see, is expressible using Schur products. As noted above, if Q and H are Hermitian and nonnegative definite their Schur product is also nonnegative definite. This is easily shown by expanding one of the factors, say H, as a sum of the form $\sum b_i b_i^{\dagger}$ and observing that for an arbitrary vector x, $x^{\dagger}(Q *$ $b_1b_1^{\dagger}x = (x * b_1)^T Q(x * b_1) \ge 0$ or by observing that $bb^{\dagger} * Q$ is actually congruent to to Q.

On to the Two-Dimensional Situation Lemma 2: Let η , b and Λ be as in Lemma 1 and let T be a nonsingular matrix. Considered as a mapping from (b, λ) to $L_2[0, \infty) \times [0, \infty)$, the Jacobian of

$$\phi(b,\Lambda)(t,\tau) = \eta e^{\Lambda t} T e^{\Lambda \tau} b$$

is

$$J(t,\tau) = \begin{bmatrix} \frac{\partial\phi}{\partial b} & \frac{\partial\phi}{\partial \Lambda} \end{bmatrix} = \begin{bmatrix} \eta e^{\Lambda t} T e^{\Lambda \tau}, & t b^T e^{\Lambda \tau} T^T e^{\Lambda t} + \tau \eta e^{\Lambda \tau} T e^{\Lambda t} * b^T \end{bmatrix}$$

Assuming that the λ_i are distinct and all components of b are nonzero, the Moore-Penrose

...and

inverse of this Jacobian maps $L_2[0,\infty) \times [0,\infty)$ to \mathbb{C}^{2n} and is given by

$$F^{-1} \int_0^\infty \int_0^\infty \left[\begin{array}{c} e^{\bar{\Lambda}\tau} T^{\dagger} e^{\bar{\Lambda}t} \eta^T \\ t e^{\bar{\Lambda}t} \bar{T} e^{\bar{\Lambda}\tau} \bar{b} + \tau e^{\bar{\Lambda}\tau} T^{\dagger} e^{\bar{\Lambda}t} \eta^T * \bar{b} \end{array} \right] (\cdot) dt \ d\tau$$

where

$$F = \int_0^\infty \int_0^\infty J^{\dagger}(t,\tau) J(t,\tau) dt \ d\tau$$

Part IV: How Much Can Control Help in Identification?

Theorem 3: Let Q and H be n by n Hermitean matrices. Let Q have diagonal entries $d_1 \ge d_2 \ge ... \ge d_n$ and let H have eigenvalues $\mu_1 \ge \mu_2 \ge ... \ge \mu_n$. The possible diagonals of the matrix $Q * U^{\dagger}HU$ as U ranges over the unitary matrices is the image of the Schur-Horn polytope defined by the eigenvalues of H under the linear transformation

$$Diag(Q) = \begin{bmatrix} q_{11} & 0 & \dots & 0 \\ 0 & q_{22} & \dots & 0 \\ \dots & \dots & \dots & \dots \\ 0 & 0 & \dots & q_{nn} \end{bmatrix}$$

The best result is obtained by matching the biggest of Q against the smallest of H, next biggest against the next smallest...
Moreover, if Q and H are nonnegative definite then

$$\max_{U} \min_{i} \lambda_{i} (Q * U^{\dagger} H U) \le \min_{i} (d_{i} \mu_{n-i+1})$$

and there exists U such that equality is achieved. Such a U can be chosen from the set of U that diagonalize H while putting the eigenvalues of $U^{\dagger}HU$ in reverse order by size as compared with the diagonals of Q.

Example

Example: To illustrate consider an example which, however, captures many of the essential features of of 2D NMR. The system has nine state variables and four resonant frequencies; no simpler model captures all the significant points. The system is described by $\dot{x} =$ $(A + uB_1 + vB_2)x + b$ with output y = cx. The vector b is the $\sqrt{2e_1}$ where e_1 is the standard basis vector and $(A+uB_1+vB_2)$ is a nine-by-nine

Example: f and f' are close, g and g' are separated

matrix

$$A+uB_{1}+vB_{2} = \begin{bmatrix} -1 & u & 0 & u & 0 & 0 & 0 & 0 & 0 \\ -u & -\sigma & f & 0 & 0 & v & 0 & 0 & 0 \\ 0 & -f & -\sigma & 0 & 0 & 0 & 0 & 0 & 0 \\ -u & 0 & 0 & -\sigma & f' & 0 & 0 & v & 0 \\ 0 & 0 & 0 & -f' & -\sigma & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\sigma & g & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\sigma & g' \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -g' & -\sigma \end{bmatrix}$$

and $y = x_6 + x_8$. The identification procedure can be described using a sequence of 5 vectors With time evolution and feedback we effect the following

followed by

$$\begin{bmatrix} 0\\ e^{-\sigma\tau} \sin f\tau \cdot e^{-\sigma t} \sin ft\\ e^{-\sigma\tau} \sin f\tau \cdot e^{-\sigma t} \cos ft\\ e^{-\sigma\tau} \sin f'\tau \cdot e^{-\sigma t} \sin f't\\ e^{-\sigma\tau} \sin f'\tau \cdot e^{-\sigma t} \cos f't\\ -e^{-\sigma\tau} \sin f\tau \cdot e^{-\sigma t} \cos gt\\ e^{-\sigma\tau} \sin f\tau \cdot e^{-\sigma t} \sin gt\\ -e^{-\sigma\tau} \sin f'\tau \cdot e^{-\sigma t} \cos g't\\ e^{-\sigma\tau} \sin f'\tau \cdot e^{-\sigma t} \sin g't \end{bmatrix}$$

 $y(t) = -e^{-\sigma\tau} \sin f\tau \cdot e^{-\sigma t} \cos gt - e^{-\sigma\tau} \sin f'\tau \cdot e^{-\sigma t} \cos g't$



2D Fourier Space

In spectroscopic applications the spreading is caused by the shielding of the magnetic field by nearby electronic spins. The extent of the shielding is is measured by the frequency shift and this, in turn, is determined by the geometry.





2D Fourier Space

In Conclusion...

Congratulations to the Honorees Alan and David.

Greetings to old friends here for the occasion.

Thanks to Albert and others involved in the organization process.

And, in affirmation of our chosen paths in life, let us hope that we can contribute, at least a modest way, to making the present century a worthy successor to the age of enlightenment.