Information Technology in Brain Intensive Therapy

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INTRODUCTION

In order to control a process, especially in a computer and instrumented assisted way, as in Brain Intensive Therapy (IT), a model of its behavior is needed. In order to do that, one must first be able to select the best set of a few (thus understandable and manageable) truly relevant variables.

In manufactured systems, also used in Brain IT, physics is in fact often quite known, with a manageable number of degrees of freedom; for instance, in robot kinematics, natural state variables may be (angular) positions and velocities.

Some natural systems are also easily characterized by state variables with physical meaning: for instance reservoirs (e.g., lakes), but also body organs with respect to soluble substances may be characterized by volumes, concentrations, fluxes, and gradients among compartments (Liberati & Turkheimer, 1999).

In other cases, the "natural" variables of the systems are not the best ones for identifying and control a process. A transformation of some of them may be needed; for instance, in the autonomous nervous control of the hearth system, the differential interbeat measure is the one that almost linearly interacts with baroreflex in the feedback control loop (Baselli et al., 1986).

In many cases, mainly for natural, especially neural processes, it is not easy to formulate a model based on variables whose physical meaning is a priori known; for instance, the electroencephalogram (EEG) is a very far field shielded measure of the interacting activity of billions of neurons. Many actors are thus playing, each one with many meaningful state variables, also depending on the investigated level, but with high reciprocal correlation. It would not be efficient to model every single variable for global monitoring such that it is not useful to take into account the kinetics of every single molecule of a gas when only global effects of pressure are of interest. A quest of some higher-level variables, even without a direct physical meaning, is thus natural in order to easily manage the complexity of the problem. Once such salient variables are found, the problem often arises to correlate in logical and/or mathematical sense their dynamics in order to properly model, forecast, and control the patient features.

Such interrelated problems will be addressed briefly in the present contribution, where Intensive Therapy is chosen as a paradigmatic application because of its critical conditions, while the approaches described whose rationale is better analyzed in the referred bibliography are of a quite general use in health information systems.

BACKGROUND

When data are in a time series (e.g., when a continuous process is properly sampled in time by an analog-to-digital converter at a sufficient frequency over the considered span of measured variables), a quite general approach is to express the measured sample $x(t)$ of each variable x as a (linear) combination of:

- The recent past $x(t-i)$ of itself;
- Possible other measured variables (which are simply taken into account in mathematical notation by considering $x(t)$ as a vector of all the considered variables);
- A superposed noise $w(t)$.

The EEG, for instance, is in fact well modeled by an autoregressive model of low order n:

$$x(t)=a(1)x(t-1)+a(2)x(t-2)+ \dots +a(n)x(t-n)+w(t)$$

The set of parameters $a(i)$, possibly varying in time, may be identified from the data time series and describes the changes in the system expressing the measured signal, whose spectrum is also easily computed from the $a(i)$ themselves.

Such a simple black box model does allow a signal identification, useful, for instance, to monitor the effects of the control procedure; EEG may then be used

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in order to monitor control of drug infusion (e.g., in anesthesia) and their effects (e.g., hypotension) even in neurosurgery (Cerutti, Liberati & Mascellani, 1985) or Brain IT. Image fluxes can be treated as a set of pixel (Liberati, DiCorrado & Mandelli, 1992) or voxel (Maieron et al., 2002) streams taking into account their correlations.

In that respect, EEG, while summarizing the behavior of the complex system from which it is derived, may be quite simply modeled, processed, and identified in order to assist control. Extraction of its salient characteristics via parametric identification and/or neural networks makes the task of classifying brain states easier; even the decision to perform may be detected (Babiloni et al., 2000) toward Brain Computer Interfacing (among the 10 emerging technologies that will change the world, according to the *MIT Technical Review* of January 19, 2004). Besides being one of the most important and complex signals to be monitored in intensive therapy, and being itself the discriminant one among life and death even on legal ground, EEG thus can be reasonably assumed as the paradigmatic example of our approach to Brain IT, even involving other signals, as described in the next section.

INFORMATION PROCESSING IN BRAIN IT

When a model describing the system has been identified (e.g., in the black box way described in the background for the EEG), a direct convolution with a known input is able to render a "clean" filtered emulation of the expected output, making easier the clinical inspection. This is interesting, for instance, for single trial-evoked and event-related brain potentials (Liberati, Bedarida, Brandazza, & Cerutti, 1991a) and useful for objective assessment of possibly noncooperating subjects.

On the contrary, when only the noisy output is measurable (e.g., in hormone blood concentration), the inverse deconvolution provides an estimate of the not directly accessible variable; for instance, pituitary secretion (De Nicolao, Liberati, & Sartorio, 2000), whose little quantity as well as its little accessibility make it of unreachable direct measure.

Correlation and coherence, even partial (Liberati, Cursi, Locatelli, Comi & Cerutti, 1997), among subsystems may be usefully identified from multiple signals, discovering, for instance:

- The cardiovascular effects of the psycho-physiological stress through neural regulation (Pagani et al., 1991)
- The integrity of even nonlinear interactions between somato-sensory and visual cortex when stimulated together (Liberati et al., 1991a)
- Brain decay in degenerative pathologies (Locatelli, Cursi, Liberati, Franceschi, & Comi, 1998), or on the opposite side, hypercorrelations such as epilepsy that could, for instance, take relief by a sort of implanted defibrillator.

Time varying coefficients may be identified via Kalman filtering (Liberati, Bertolini, & Colombo, 1991b). Higher order spectral correlation also may be identified through a parametric approach, leading, for instance, to identify nonlinear effects as in muscle contraction (Orizio, Liberati, Locatelli, DeGrandis, & Veicsteinas, 1996) or in neural plasticity (Locatelli et al., 1986).

Nonetheless, linear, time invariant, and even multivariable modeling do allow much easier theory and algorithms, and thus more understandable results than nonlinear and time varying approaches. A natural quest is thus to approximate nonlinear models to linear ones in different regions. The problem is that it is not easy to a priori know-how to partition such regions. A possible solution (Ferrari-Trecate, Muselli, Liberati, & Morari, 2003) automatically clusters data in regions, without imposing continuity even in the variables at the borders, within the framework of the dynamic-logical "hybrid" models. In such a way, a linear regression is then jointly estimated in each region. Switching and nonlinear models thus may be simply identified via such Piece Wise Affine identification approach obtained by complementing a modified version of the cited stochastic parametric identification algorithm with a slightly modified *k-means* clustering. Most of the previously cited results can thus be revisited with such an approach. For instance, hormone pulses during secretion may be detected as belonging to one of the two identified states, the other being quiescent. In the same way, brain states can be discriminated, as in sleep staging.

When time course is not of paramount relevance to the data set, clustering becomes the only focus of the processing toward selecting salient variables and possibly identifying logical relationships among them. When many variables, even not homogeneous, are available, as in Brain IT, a simple hierarchy according

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