Expert Adaptive Control
for Drug Delivery Systems

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ABSTRACT: The goal of this investigation is the development of an adaptive drug delivery system for use in regulation of critical care patients suffering from cardiac failure. The approach taken here assumes that adaptive control algorithms combined with expert system techniques are necessary to maintain stable patient status within narrow physiological bounds in the presence of large plant uncertainties. To this end, a hybrid controller is presented whose structure is adjusted by an expert system that attempts to match the best control scheme in accordance with the dynamic structure of the plant. An illustrative example is presented, demonstrating the improved performance provided by the hybrid control scheme.

Introduction

The goal of this work is the development of an automated drug delivery system for the treatment of critically ill patients with cardiac failure in order to reduce the work load of the attending personnel. Many factors contribute to the fact that the regulatory challenge faced by such a controller is a difficult one. These include: unmodeled dynamics of the plant, time-varying nature of plant parameters, nonlinearities and cross interaction of drug responses, narrow bounds of stable existence, and the inherent time delays of the patient's response to the drug infusion. The evolution of control schemes for tackling such problems is demonstrated by a non-adaptive blood pressure controller [1], an adaptive blood pressure controller [2], an adaptive blood pressure and cardiac output controller [3], and an adaptive arterial pressure and central venous pressure controller [4]. However, these approaches have been plagued by problems, which include the question of stability of adaptive controllers applied to plants with unmodeled dynamics [5], deterioration of controller performance in the presence of poor parameter estimates, the need for an initial parameter estimation period, and failure to apply the controller to the targeted "sick heart" condition, where such a scheme would serve its purpose.

The next stage in the evolution of a control approach would be to allow the controller structure to change in order to accommodate the possible variation undergone by the plant. This type of controller, which expands the capabilities of conventional controllers, requires logic in the form of a supervisor or expert to orchestrate the controller structure as the conditions of the process change. Expert control concepts have been introduced previously to coordinate parameter adaptive control methods [6], [7]. An example of these concepts applied to a fuzzy control approach in the regulation of a servomotor is given in [8].

The major contribution of this paper is a new automated adaptive control scheme, which consists of a bank of control algorithms whose coordination and system stability assessment is orchestrated by a supervisory system. The hybrid control structure presented here ranges from a crude control scheme, where the actions of the operator are represented in a rule-based format, to a model-based adaptive approach, where the output of the plant is forced to follow the output of a desired reference model. The design of each individual controller is based on the "rules of thumb" that experts use in controlling poorly modeled processes to be encoded in a systematic manner. Thus, the application of a fuzzy controller to regulating a process is ideal when little is known about the plant and the goal is to model the actions of the expert. For the process presented here, the expert is the physician.

The fuzzy controller approach is successful in moving the state of the plant toward the set point, but once close, a steady-state oscillation frequently occurs about the set point arising from the nonlinear nature of the algorithm. In the proposed structure, this
Multiple-Model Adaptive Control

The next level in this hierarchical control structure uses a dramatically different control scheme from that of the coarse fuzzy control approach. In contrast to modeling the operator, this method classifies the plant as one model out of a bank of predefined models and implements a controller designed about that nominal model. This adaptive approach is known as multiple-model adaptive control. A bank of models with constant parameters is predefined so as to span the range of parameter variation expected by the plant. Calculated residuals represent the difference between each model in the bank and the plant in response to the same applied control value. Each model in the model bank has a corresponding controller in the controller bank designed so that each controller-model pair meets specified design criteria. The actual control value applied to the plant and model bank is composed of a weighted combination of the controller bank outputs. The algorithm for determining the weights is given in [2]. The resulting control value, $u_c$, is given in Eq. (1), where $u_i$ is the individual controller value, $W_i$ the corresponding weighting factor, and $n$ the number of model-controller pairs in the model bank.

$$u_c = \sum_{j=1}^{n} W_j u_j$$  \hspace{1cm} (1)

In the ideal case, the plant would match a particular model in the model bank, and the resulting closed-loop system would meet precisely the predetermined design specifications. In actuality, there is a range of responses for a plant within one parameter space. The coarseness of the model bank dictates the ultimate performance of the controller.

Model Reference Adaptive Control

The finest tuning calculation by the hybrid controller is the direct model reference adaptive controller. This method, as derived from command generator tracker theory [11], directly calculates the control value without explicit knowledge of the plant parameters. The controller forces the plant to follow a reference model containing the desired system dynamics. The control value, $u_c$, is determined by a linear combination of the error between the plant and reference model, $y_p - y_r$, the reference model states, $x_m$, and the command signal to the reference model, $u_m$, as shown in Eq. (2).

$$u_c = K_s (y_p - y_r) + K_x x_m + K_u u_m$$  \hspace{1cm} (2)

Application of model reference adaptive controllers requires that the process meets specific sufficient conditions. For this algorithm, the characterization of the plant as strictly positive real is the issue regulating the bounds on allowable plants. There have been two basic approaches taken in the effort to extend the class of allowable plants to which the model reference controller may be applied. One method is to augment the plant with either an inner loop [12] or a feedforward filter [13]. A second approach is to change the form of the control laws.

The hybrid controller presented here uses both of these ideas in dealing with the sufficiency conditions required by the model reference controller. The classification of the plant into a specific parameter space allows for a corresponding adjustment in the model reference control laws. In addition, the compensation provided by the multiple-model controller results in an augmented inner loop, which helps meet the conditions required by the model reference controller.

Expert System

The expert system orchestrates the operation of the hybrid controller in accordance with the dynamic plant. This element allows for a systematic approach in dealing with heuristic decisions involved in determination of the proper controller. Many approaches to representing knowledge in the expert system format exist [14]-[16]. The approach used here is that of a production system or rule-based expert system, whose major components are rule base, inference engine, and data base.

The data base contains both static and dynamic elements describing the present state of the system. Static data include thresholds to determine convergence of algorithm parameters [i.e., the weights in Eq. (1)]. Dynamic data consist of real-time values characterizing the present state of the plant and controller operation (i.e., the error and change in error of the regulated variables). The rule base contains rules in the "if (case) then (action)" format, which deal with conditions involving changing control schemes. The premises of the rules deal with conditions on the present data and control structure.

A backward chainer performs the inference function for this production system. This approach assumes a goal such as "The controller is the model reference controller" and tries to prove it using the data base and rule base.

This approach to representing the heuristics of the decision process allows for automatic intelligent decision making as opposed to preprogramming logic, which treats each case individually.

Summary of Method

The complete hybrid control structure is shown in Fig. 2. The system builds on itself in a "learning"-type manner. At the outset of the controller operation, when the system knows nothing about the patient, the fuzzy controller provides the initial crude control by imitating the actions of the physician (switch in position 1). This initial infusion rate allows the multiple-model adaptive controller to determine which model in its model bank most closely matches the patient’s dynamic response. Control switches to the multiple-model controller when the expert system determines that conditions warrant the change. At this point, the compensator determined a priori for the chosen model dictates the drug infusion rate (switch in position 2). The multiple-model controller and plant at this stage become an inner loop (outlined) for the model reference adaptive controller in order to satisfy sufficiency conditions for its application. The final switch, as determined by the expert system, allows the model reference controller to adjust in a fine-tuning manner the reference signal to the inner loop in order that the patient follows the desired trajectory given by the reference model (switch in position 3). With this hierarchical control structure, the system accommodates an adaptive reference model selection process, as shown in Fig. 3. The dynamics of the reference model are a function of the multiple-model classification of the patient. The system is designed so that a patient with slow dynamics will not be forced to follow a fast model, and a patient with fast dynamics will not be forced to follow a slow model. Once the multiple-model controller converges on a model-controller pair, this nominal closed-loop system becomes the reference model for the augmented plant to follow. The compensator, as selected by the multiple-model approach, and the plant together become the augmented plant for the model reference controller. Once the expert system warrants the advancement of the system to the model reference stage, this controller will stay in command until the model reference gains inflate excessively or the plant output strays too far from the set-point value. In this case, the system will return to the multiple-model controller—or perhaps the fuzzy controller—
for infusion rates and then repeat the process by determining a new augmented inner-loop configuration more suitable for the plant state.

Illustrative Example

The performance of the hybrid controller was tested in simulations by comparing its regulatory abilities to the individual controllers that make up its structure in the regulation of blood pressure. The model used as the plant is given in Eq. (3) and represents the transfer function between the change in blood pressure in response to sodium nitroprusside infusion [17]. The parameter values used were $\tau_p = 60$ sec, $T_d = 50$ sec, with $k$ a function of time, as shown in Fig. 4.

$$G(s) = \frac{k \exp (-T_{\text{delay}})}{(\tau_p s + 1)}$$  \hspace{1cm} (3)

The variable gain, which models the patient's decrease in sensitivity to the drug, and the time delay represent two characteristics that make this a challenging control problem.

In this simulation, a comparison is made between the regulatory ability of the fuzzy controller, the fuzzy controller plus the multiple-model controller, and the entire hybrid structure (fuzzy controller plus multiple-model controller plus model reference controller). The fuzzy controller rules were generated by asking physicians what infusion rates of sodium nitroprusside they would use in treating a spectrum of dynamic blood pressure conditions. The model-controller pairs in the multiple-model controller were a priori designed [2] to control a plant such as in Eq. (3), exhibiting a variable-gain behavior ranging from $k = -0.3$ to $-8.0$. The reference model in the model reference controller was the closed-loop system formed by the chosen multiple-model compensator with its corresponding nominal model. The results are shown in Fig. 5.

The dotted line at the base of the figure signifies when the expert system chose to switch between different control schemes. The simulation demonstrates that the complete hybrid structure yields superior regulation ability. The fuzzy controller alone displays the difficulty that humans have in regulating systems with time delays and parameter variations. However, in the hybrid control structure, the fuzzy controller action

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Fig. 2. Block diagram of complete hierarchical control system.

Fig. 3. Block diagram of the highest stage of the controller, where the multiple-model adaptive controller (MMAC) configures the structure of the reference model and the augmented plant.

Fig. 4. Plot of time-varying gain used in the simulation.

Fig. 5. Plot of simulation results: -- , fuzzy controller; . . . . , multiple model + fuzzy controller; - - - - , model reference + multiple model + fuzzy controller; - - - - - , hybrid controller stages: I, fuzzy controller; II, multiple model; III, model reference.
provides gross adjustments to attain the state of the system near the set point, while simultaneously giving a signal to the multiple-model controller to search its model bank in order to find the closest linear compensator for the given plant. With the multiple-model controller in charge, the system attains the best performance for the given plant. With the multiple-model controller in charge, the system attains the best performance for the given plant.

Controller. However, the multiple-model approach has difficulty dealing with the parameter variation, as seen by the glitch in the response caused by the plant moving from one model space to another. The model reference controller, with its ability to regulate plants containing unmodeled dynamics, requires more fine-tuning control when the plant moves from one operating point to another. The model reference controller, with its ability to regulate plants containing unmodeled dynamics, requires more fine-tuning control when the plant moves from one operating point to another.

Conclusion
An expert hybrid control scheme, without the use of parameter estimation techniques, has been presented, which adjusts its structure in order to provide the best control for a broad range of plant conditions. Three control procedures, ranging from a coarse control action (fuzzy control) to a fine-tuning control (model reference control), are uniquely combined to improve the regulation abilities of each controller individually. The contention is that adaptive techniques combined with expert system ideas are necessary in order to meet the challenging regulatory needs of drug delivery systems. The worst case, this system will perform as well as the physician; at best, the patient’s state will be driven to the desired set point in a manner as prescribed by the reference model. Further investigations will involve testing the system with a multiple-input/multiple-output plant, where the expert system will require an enhanced rule base in order to orchestrate the controller structure.

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References

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