A Robust Temperature Controller Design for an Innovative Hyperthermic Intraperitoneal Chemotherapy Equipment

Iulia Clitan[1], Corneliu Lungoci[2], Vlad Muresan[1], Daniel Moga[1] and Valentin Sita[1]
[1]*Department of Automation, Technical University of Cluj-Napoca, 26-28 Baritiu Street, Cluj-Napoca, Romania*
[2]*Department of Surgery, "Iuliu Hatieganu" University of Medicine and Pharmacy, 8 Victor Babes Street, Cluj-Napoca, Romania*

Keywords: Cytoreductive Surgery, Regional Chemotherapy, Hyperthermic Intraperitioneal Chemotherapy (HIPEC) Equipment, Temperature Control, Strejc Identification Method, Robust Control, H∞ Controller.

Abstract: This paper presents an advanced control structure for controlling the heating process of cytostatic solution used in regional chemotherapy. The solution temperature control is an individual control structure which is desired to be implemented on hyperthermic intraperitioneal chemotherapy (HIPEC) innovative device. Cytoreductive surgery followed by HIPEC represents a therapeutic solution for patients suffering from peritoneal carcinomatosis, an abdominal cancer. An H∞ robust control structure is designed since the heating process model's parameters depend on the solution's delivery flow. It is considered that the heating process gain can vary from a nominal value to a maximum value, which represents an increase by up to 100% from the nominal value. The responses to a step input signal for the nominal case, and the cases when the gain varies by 50% or 100%, are simulated. The control structure is compared against a PID feasible controller by means of overall performances. It resulted that the robust controller generates the best performance set for the nominal gain and also for the case when the heating process gain varies.

1 INTRODUCTION

Peritoneal Carcinomatosis (PC), together with the hepatic metastases was related in the past to the final stage of cancer, being considered a surgically incurable pathological state (Koppe et al, 2006). The standard treatment, the systemic chemotherapy, for this stage of the disease was not an efficient solution because of the high tumor volume and the biological exhaustion of the organism (Gleben et al, 2010). The excess of mortality and morbidity due to cancers is a reality that motivates consistent research and development efforts aimed at solving these issues. Cytoreductive surgery and regional chemotherapy: the intensification of the cytostatic drugs effect through the association of hyperthermia (delivered at a high temperature of 41-43˚C), makes hyperthermic intraperitioneal chemotherapy (HIPEC) a technique that allows approaching PC in a therapeutic manner (Levine et al, 2012; Sugarbaker and Clarke, 2006).

In the last years this radical therapeutic approach for selected PC patients, through cytoreductive surgery followed by HIPEC represents a standard treatment (Sugarbaker, 2012). The procedures are still in a more or less experimental phase, mainly due to cost and technical limitations of the current equipment and lack of appropriate monitoring. There are few HIPEC devices commercially available, for the delivering of the cytostatic drugs at the required temperature, like ThermoChem HT-2000, Cavitherm EFS 0685, SunChip or Anti-Meta. The HIPEC devices based on the accepted Spratt model basic architecture consists in peristaltic pump, heat exchanger, temperature, pressure and flow sensors and a storage reservoir (Spratt et al, 1980; Sugarbaker, 2005). Some of the technical limitations of the commercially available equipment are the absence of a distributed temperature monitoring system (able to provide comprehensive information regarding the intraperitoneal temperature distribution), the decreased number of delivery channels (two inflow lines), or the absence of advanced control algorithms (classical control structures are used in order to ensure a homogenous temperature in the peritoneal cavity at a constant flow rate).

The authors are developing a HIPEC equipment that offers: a complex solution distribution system

Clitan I., Lungoci C., Muresan V., Moga D. and Sita V..
A Robust Temperature Controller Design for an Innovative Hyperthermic Intraperitoneal Chemotherapy Equipment.
DOI: 10.5220/0005543800840091
In *Proceedings of the 12th International Conference on Informatics in Control, Automation and Robotics* (ICINCO-2015), pages 84-91
ISBN: 978-989-758-123-6

with multiple nozzles; a multipoint temperature measurement system; smart control algorithms for localized flow and temperature control. In the social and economic context, an affordable equipment for HIPEC has a real implementation potential in all cancer treatment centers, thus the cost of the equipment is the main focus of the authors. The pourpose is to create a functional and innovative equipment that overcomes the previously stated limitations of the HIPEC equipments.

The most suitable architecture for the proposed HIPEC equipment was presented in (Lungoci et al, 2014; Stroia et al, 2014), and some of the essential components of the equipments architecture are indicated in figure 1, where:

- *FC* – represents the flow controller, used in order to maintain a constant delivery flow of the solution since the delivery flow varies between 0.1 – 0.2 liters/minute;
- *HC* – represents the individual heating controller used in order to maintain the temperature of the solution in the range of 41-43˚C;
- *TS* – represent temperature sensors that measure the temperature of the solution at the output of the preheating tank, and also the temperature of the solution after the heating element;
- *FRS* – represents the flow rate sensors;
- *Storage tank* – used in order to store and to preheat the cytostatic solution at a temperature of 38˚C;
- *Supply and return pump* – ensure the circulation of the solution from the storage tank to the patient cavity, and back;
- *Individual heater* – a heating resistance constructed as windings on the exterior wall of a cylindrical tube trough which the solution is circulated (see figure 2), that works on the principle of a heat exchanger;

The temperature sensors used for the implementation of the HIPEC equipment's temperature monitoring system are PT 1000, such a sensor is presented in figure 3.

The equipment architecture presented in figure 1 contains only one delivery channel. On the final HIPEC equipment the authors are going to use a number of up to eight delivery channels that are going to have the same individual elements presented above. The number of channels was chosen by the authors in terms of delivery and optimal homogenization of the solution inside the peritoneal cavity (Lungoci et al, 2014; Stroia et al, 2014).

In this paper the authors present the design of an advanced automatic temperature control structure capable of maintaining the required temperature for the cytostatic solution.

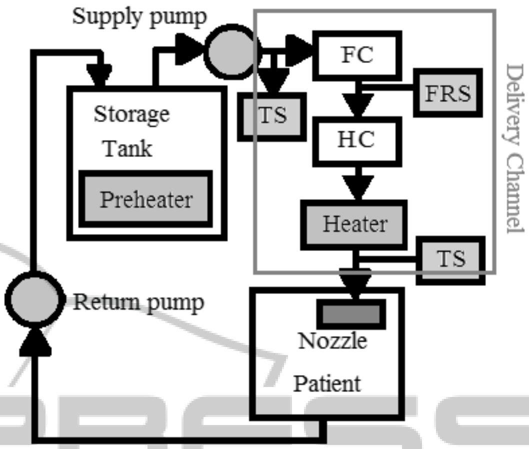

Figure 1: The HIPEC equipment components.

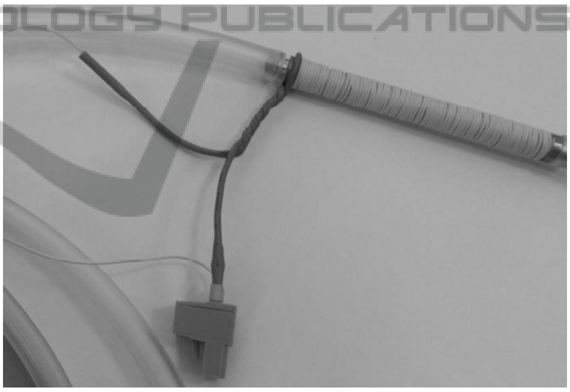

Figure 2: The individual heater.

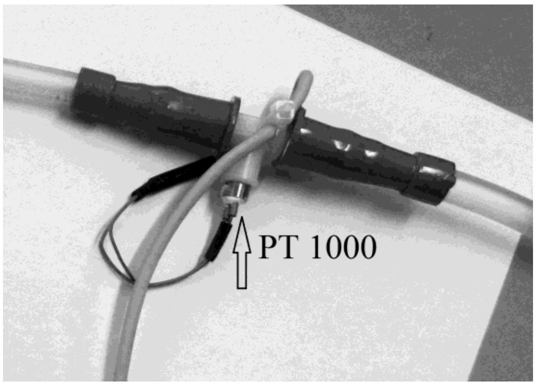

Figure 3: The PT 1000 temperature sensor.

The case where a H_∞ robust controller is used in order to control the solution's temperature is studied. The robust control is selected since the heating process model's parameters depend on the cytostatic solution's flow rate.

2 MATHEMATICAL MODEL OF THE HEATING PROCESS

2.1 The Transfer Function Model

The mathematical model of the heating process is obtained by using a graphical fitting method on a set of experimental data. The experimental data plotted in figure 4 represents the solution's temperature at the output of the heating element, measured at a step type input signal and at a constant solution flow of 0.1 litres/ minute. The heating process input signal is represented by the electric power used to heat the heating element. The step response for the heating system was achieved by applying a constant electric power of 15.5 watts to the heating element, without the pre-heater associated to the storage tank. This means that the initial temperature of the solution, for the experimental data from figure 4, is the temperature of 15˚C instead of 38˚C.

In order to obtain a transfer function model the Strejc identification method was applied, on the basis of the shape of the experimental data set. The method was explained in detail in a related work (Clitan, 2015). The identification method consists in approximating the heating system through a transfer function of the following form:

$$H_{HP}(s) = \frac{k_{HP}}{(1+T_{HP}s)^n} \tag{1}$$

where n is the order of the process, k_{HP} represents the heating system gain, and T_{HP} represents the heating system time constant.

The order of the process and the heating system time constant are obtained based on the correlation between a series of calculated ratios and the Strejc identification table (Mikleš and Fikar, 2007). The corresponding ratios are calculated based on some time periods determined graphically, in respect to a tangent line drawn in the experimental signal's inflection point.

Following the identification method, a third order transfer function with a time constant equal to 17 seconds results as the mathematical model for the heating process.

The heating process gain (k_{HP}) is determined using the steady state temperature value (t_{ss}) of 19.2˚C and the offset temperature value (t_o) of 15˚C (see figure 4).

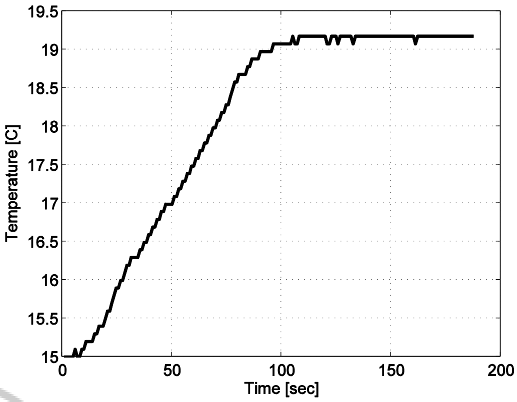

Figure 4: The temperature experimental data.

$$k_{HP} = \frac{t_{ss} - t_o}{u_{ss} - u_o} = \frac{19.2 - 15}{15.5 - 0} = 0.271 \tag{2}$$

The value of the heating process gain will be the same regardless of the temperature offset, since if that value changes than the steady state temperature value will also change accordingly, as long as a constant solution flow rate and electric power is supplied.

The heating process mathematical model is obtained as the transfer function given below in (3). The model validation is presented in figure 5 where the simulated model's step response is plotted in respect to the experimental data set.

$$H_{HP}(s) = \frac{0.271}{(1+17s)^3} \tag{3}$$

The heating process gain depends on the solution's flow value, since the output temperature value varies with the flow. If the solution's delivery flow doubles in value (the maximum value of the flow rate is 0.2 liters/minute) then the system gain also doubles.

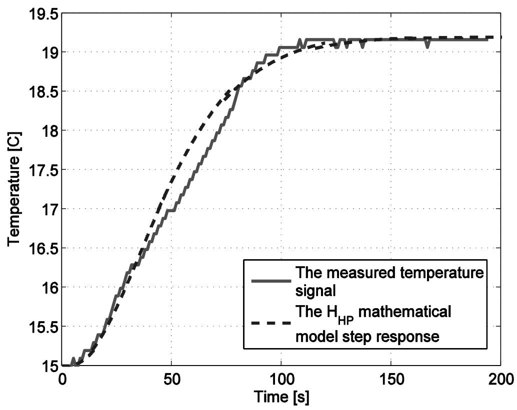

Figure 5: The heating process model validation.

The control signal for the supplied electrical power is applied using Pulse-width modulation (PWM). The PWM transfer function has a gain equal to 30. This gain needs to be added to the heating process transfer function (H_{HP}) and the resulted fixed part transfer function (H_{FP}) is given in (4).

$$H_{FP}(s) = \frac{30 \cdot 0.271}{(17s+1)^3} = \frac{8.13}{4913s^3 + 867s^2 + 51s + 1} \quad (4)$$

2.2 The State Space Representation of the Model

The heating process fixed part model can also be represented by using the state space representation given in (5).

$$\begin{cases} \dot{x}_1(t) = -0.1765x_1(t) - 0.01038x_2(t) \\ \qquad - 0.0002035x_3(t) + v(t) \\ \dot{x}_2(t) = x_1(t) \\ \dot{x}_3(t) = x_2(t) \\ z(t) = 0.001654x_3(t) \end{cases} \quad (5)$$

where $x_i(t)$ represent the state variables, $z(t)$ represent the output temperature and $v(t)$ represent the input.

The state matrix, the input matrix, the output matrix and the feedthrough matrix are presented below in (6), (7), (8) and (9) correspondingly.

$$A = \begin{bmatrix} -0.1765 & -0.01038 & -0.0002035 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \end{bmatrix} \quad (6)$$

$$B = \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix} \quad (7)$$

$$C = \begin{bmatrix} 0 & 0 & 0.0061 \cdot 0.271 \end{bmatrix} \quad (8)$$

$$D = 0 \quad (9)$$

3 ROBUST CONTROLLER DESIGN

3.1 The H∞ Robust Control

The main goal of a robust control is to design a controller that stabilizes the process not only for its nominal parameters values but also for the case in which the parameters vary within a certain range (Szelitzky et al, 2011). Such a control structure ensures robust performance in response to parameter uncertainty (Doyle et al, 1989). When using a robust control structure the controlled process will have the following requirements: low overshoot, short settling time and disturbance rejection (Inoan, 2011). Thus an H∞ robust control is used for the temperature control of the HIPEC equipment heating process.

The H∞ robust control design consists in finding a controller that minimizes the lower linear fractional transformation for the heating process fixed part (Damen and Weinland, 2002).

In order to design an H∞ robust controller the augmented plant mathematical model (G) described in (10) has to be constructed. This matrix form is obtained from the state space representation which includes the exogenous inputs and the error signals (Inoan, 2011).

$$G = \left[\begin{array}{c:c:c} A & B_1 & B_2 \\ \hdashline C_1 & D_{11} & D_{12} \\ \hdashline C_2 & D_{21} & D_{22} \end{array}\right] \quad (10)$$

3.2 The Robust Controller for the Heating Process

The H∞ controller design for the heating process begins with the state-space representation of the fixed part described in (5). Figure 6 shows the block schematic representation of the fixed part state space representation.

The heating process model's parameters, namely the process gain, depend on the cytostatic solution's flow rate since the heating process of the solution depends on the amount and speed of the solution. These values are set through the flow generated by the supply pump.

As stated before the gain of the heating process is influenced by the amount of solution flow. The solution flow can vary between 0.1 – 0.2 liters/minute, thus the gain value can vary between 0.271 (considered to be the nominal value) and 0.542, which means that the parameters k_{HP} varies by +100%.

The parameter k_{HP} may be represented as a lower linear fractional transformation using the relative variation $\delta_k \in [0,1]$ and the matrix M_k given in (11).

$$M_k = \begin{bmatrix} 0 & k_N \\ p_\omega & k_N \end{bmatrix} \quad (11)$$

were p_k is the maximum relative uncertainty (in this case equal to 1), and k_N is the nominal value of the heating process gain.

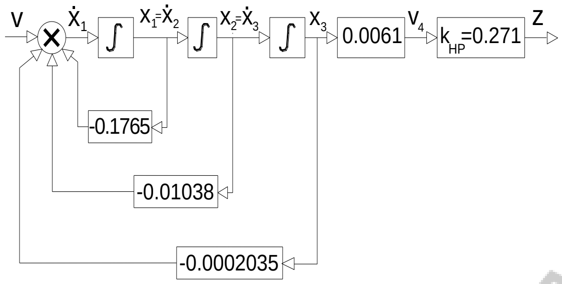

Figure 6: The block schematic representation of the fixed part state space model.

Using the lower linear fractional transformation the uncertain parameter block k_{HP} from figure 6 is going to be replaced with the group of blocks presented in figure 7.

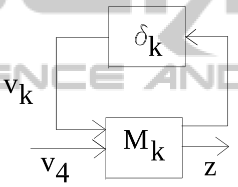

Figure 7: The heating process model validation.

The equations corresponding to the block representation given in figure 7 are:

$$\begin{aligned} z_k &= k_N v_4 \\ z &= p_k v_k + k_N v_4 \end{aligned} \tag{12}$$

were v_k represents the exogenous input and z_k represents the error signal.

The dynamic behaviour of the heating process with the uncertain parameters is described by the system equations given in (13).

$$\begin{cases} \dot{x}_1(t) = -0.1765x_1(t) - 0.01038x_2(t) - \\ \qquad - 0.0002035x_3(t) + v(t) \\ \dot{x}_2(t) = x_1(t) \\ \dot{x}_3(t) = x_2(t) \\ z_k(t) = 0.271 \cdot 0.0061x_3(t) \\ z(t) = 0.001654x_3(t) + p_k v_k(t) \end{cases} \tag{13}$$

In order to obtain the augmented plant mathematical model matrix form, the state space representation from (13) must be written as (14), having one exogenous input and one error signal.

$$\begin{cases} \dot{x}(t) = Ax(t) + B_1 v_k(t) + B_2 v(t) \\ z_k(t) = C_1 x(t) + D_{11} v_k(t) + D_{12} v(t) \\ v(t) = C_2 x(t) + D_{21} v_k(t) + D_{22} v(t) \end{cases} \tag{14}$$

The matrix form of the augmented plant model is presented in (15).

The robust controller is designed in order to minimize the error signal using the command *hinfsyn* from MATLAB® and the augmented plant model given in (15) (Gu et al, 2005).

$$G = \left[\begin{array}{ccc:c:c} -0.1765 & -0.01038 & -0.0002035 & 0 & 1 \\ 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ \hdashline 0 & 0 & 0.001654 & 0 & 0 \\ \hdashline 0 & 0 & 0.001654 & 1 & 0 \end{array}\right] \tag{15}$$

In order to ensure good transient response the following weighting functions were added (Gu et al, 2005).

$$\begin{aligned} W_p &= 0.3\frac{s^2 + 5s + 10}{s^2 + 2s + 0.0001} \\ W_u &= 0.02 \end{aligned} \tag{16}$$

The H_∞ robust controller's transfer function is obtained from the matrix form by using the formula given in (17) (Ogata, 2009). The resulted controller's fifth order transfer function is presented in (18).

$$H_f(s) = C(sI - A)^{-1}B \tag{17}$$

$$H_{RC}(s) = \frac{n_1 s^4 + n_2 s^3 + n_3 s^2 + n_4 s + n_5}{s^5 + d_1 s^4 + d_2 s^3 + d_3 s^2 + d_4 s + d_5} \tag{18}$$

were

$$\begin{aligned} n_1 &= 3.206 \cdot 10^5 \\ n_2 &= 7.068 \cdot 10^5 \\ n_3 &= 1.181 \cdot 10^5 \\ n_4 &= 6814 \\ n_5 &= 132.3 \\ d_1 &= 1501 \\ d_2 &= 5211 \\ d_3 &= 5968 \\ d_4 &= 3081 \\ d_5 &= 0.154 \end{aligned} \tag{19}$$

4 SIMULATION RESULTS

The temperature control structure previously designed is analyzed based on its simulated step response using MATLAB® Simulink, since the experimental results will be obtained for a forthcoming paper. A negative feedback control structure is implemented using the controller's transfer function given in equation (17) and the transfer function given in (4) for the PWM actuator and the heating process to be controlled.

The H_∞ robust control structure is first simulated using the nominal value for the heating process gain. The step response for the nominal case is presented in figure 8.

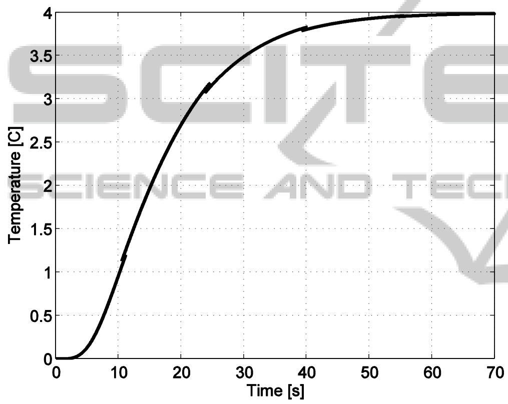

Figure 8: The H_∞ robust controller's step response for the nominal case.

The cytostatic solution's heating process is simulated over the temperature of 38˚C (the preheated solution's value) thus in order to heat the solution to a temperature of 42˚C a temperature reference signal of 4˚C is used in simulation. On the step input signal a second order delayed element of 15 seconds is used.

The overall performances for the nominal case are: zero steady state error, no overshoot and a settling time of 49 seconds. In figure 9, along with the step response for the nominal case, the step responses for the cases when the gain's value is increased by 50% and by 100% are also plotted.

It can be observed that no steady state error and no overshoot are obtained even if the value of the gain varies. The settling time when the heating process gain is increased by 50% is equal to 48 seconds, and the settling time when the gain is increased by 100% is 47.5 seconds.

The robust controller is compared with a PID controller designed using the Strejc design method (Clitan, 2015). A first order filter was added to the PID controller in order to have a feasible controller and the PID controller's transfer function is given in (20). The two controllers are compared based on their step responses for the nominal case and the case when the system's gain varies by 50% or by 100%, those step responses are presented in figure 10.

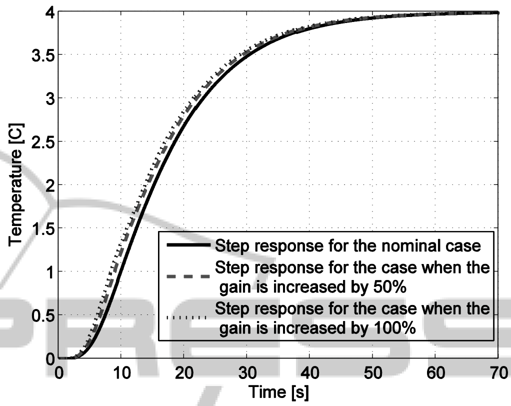

Figure 9: The H_∞ robust controller's step responses for the heating process gain nominal value, the case when the gain is increased by 50% and also by 100%.

$$H_{PID} = \frac{0.2844\left(1 + \frac{1}{41.933s} + 0.6486s\right)}{\left(0.006486s + 1\right)} \tag{20}$$

From the analysis of figure 10 it results that the performances generated by the robust controller are much better than those obtained when using the PID controller, designed using Strejc method. With the PID controller an underdamped step response is obtained having a high overshoot of 38% and a settling time of 270 seconds, for the nominal case. Even if we adjust the PID parameters so as to obtain better performances, the step responses would still change if the process parameters vary from the nominal values.

Since the robust controller is faster and has no overshoot, meaning that the solution is heated only at the desired temperature, this control structure is chosen as the most suitable one for the temperature control of the developed HIPEC equipment.

In figure 11 the control signals generated by the robust controller in order to obtain the step responses presented in figure 9 are depicted. The negative values for the control signals are not a problem since in order to ensure the initial conditions a default level of electric power is ensured.

The robust control law is going to be implemented on a microcontroller by computing the

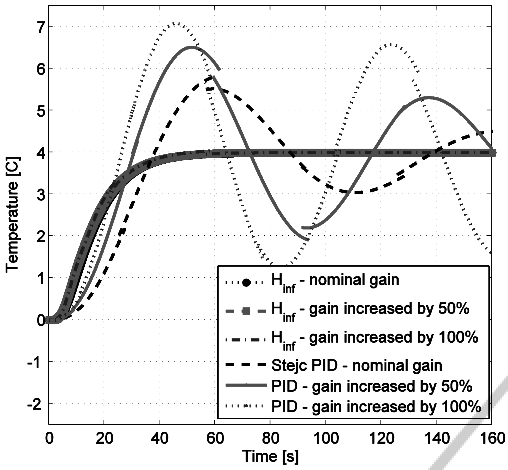

Figure 10: The graphical comparison between the H∞ robust control structure and a PID control structure for the nominal case and the case when the gain is increased by 50% and by 100%.

control signal according to the discrete-time algorithm given below.

$$\begin{aligned} c_k &= 2.965c_{k-1} - 2.93c_{k-2} + 0.9653c_{k-3} + \\ &+2.22\cdot 10^{-16} c_{k-4} - 5.551\cdot 10^{-17} c_{k-5} + \\ &+0.1681e_{k-1} + 0.1681e_{k-2} - 1.319e_{k-3} + \\ &+1.301e_{k-4} - 0.1595e_{k-5} - 0.1595e_{k-6} \end{aligned} \tag{21}$$

where c_k represents the current value of the control signal that need to be computed, c_{k-1}, c_{k-2}, c_{k-3}, c_{k-4}, c_{k-5} represent past values of the control signal and e_{k-1}, e_{k-2}, e_{k-3} e_{k-4} e_{k-5} e_{k-6} represent past values of the temperature error signal.

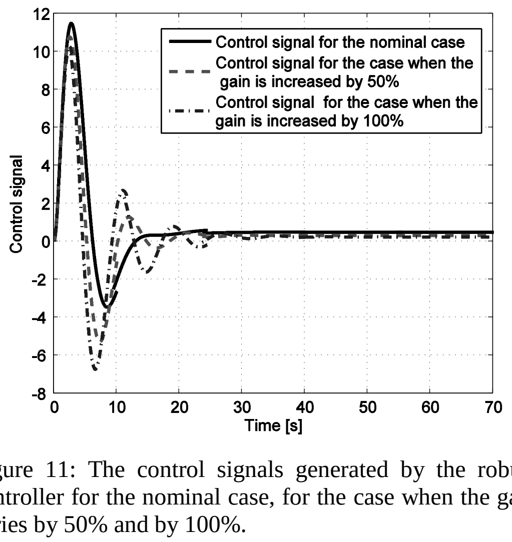

Figure 11: The control signals generated by the robust controller for the nominal case, for the case when the gain varies by 50% and by 100%.

The advantage of using the designed robust controller is that it stabilizes and generates suitable performances for the heating process not just for the nominal value of the heating process gain, but also for the case in which the gain varies. The gain variation is due to the solution's flow rate and it was shown that this control structure generates similar overall performances even if a constant solution' flow is not provided.

This means that by using a robust temperature controller the flow control structure is no longer necessary, thus reducing the cost of the HIPEC equipment since up to eight individual flow control structures would be eliminated.

5 CONCLUSIONS

The authors design in this paper a temperature control structure for the cytostatic solution heating process, so as to obtain affordable HIPEC equipment. A disadvantage of commercially available HIPEC equipments is their high cost and the fact that they do not have advanced control structures.

A robust control structure is selected since the heating process model's parameters depend on the cytostatic solution's flow rate, namely the heating process gain. A H∞ controller is designed using MATLAB. From simulation it was deducted that the robust control structure generates similar overall performances for the nominal case, and also for the case when the heating process gain varies by +50% or by +100%. A zero steady state error, no overshoot and a settling time of about 50 seconds are obtained for the cytostatic solution heating process even if the solution's flow varies.

The robust control structure was compared with a PID control structure, obtained using Strejc design method. Unlike the robust control the PID control generates worst performances even for the nominal case, in which we have a constant flow of 0.1 liters/ minute.

The advantage of using the designed H∞ robust controller is that it reduces the number of controllers needed on the HIPEC device. A flow control structure is no longer necessary since it was shown that the robust controller maintains the required temperature even if the solution flow is not constant. This means that flow rate sensors are also no longer necessary.

By implementing the robust controller designed in this paper the cost of the HIPEC equipment is reduced since up to eight individual flow control structures would be eliminated.

ACKNOWLEDGEMENTS

The research activity that helped the authors to elaborate the paper is sponsored by the research projects no. 30104/2014 and no. 30141/2014, financed by the Technical University of Cluj-Napoca.

REFERENCES

Clitan, I., Muresan, V., Moga, D., Sita, V., Lungoci, C., July 2015. Measured signal identification and temperature controller design for a HIPEC device. *38th International Conference on Telecommunications and Signal Processing TSP*, Prague, Chech Repuplic, in press.

Damen, A., Weinland, S., 2002. *Robust control*. Eindhoven University of Technology. Eindhoven, Chapter 7.

Doyle, J., Glover, K., Khargonekar, P., Francis, B., 1989. State-space solutions to standard H-2 and H-infinity control problems, *IEEE Trans. Auto. Control* 34 (8), pp. 831-847.

Gleben, O., Gilly, F. N., Arvieus, C., Cotte, E., Boutitie, F., Mansvelt, B., Bereder, J. M., Lorimier, G., Quenet, F., Elias, D., 2010. Peritoneal carcinomatosis from gastric cancer: A multi-institutional study of 159 patients treated by cytoreductive surgery combined with perioperative intraperitoneal chemotherapy, *Annals of Surgical Oncology* 17, pp. 2370-2377.

Gu, D. W., Petrov, P. H., Konstantinov, M. M., 2005. *Robust control design with Matlab,* Springer-verlag. London, Chapters 4 and 8.

Inoan, I. , Abrudean, M. , Szelitzky, T., 2011. Robust H_∞ position control of an unloading machine from a rotary hearth furnace, *Scientific bulletin of the Petru Maior University of Târgu Mureș*, 8 (2), Petru Maior University Publisher, Targu Mures, pp. 38-43.

Koppe, M. J., Boerman, O. C., Oyen, W. J. G., Bleichrodt, R. P., 2006. Peritoneal carcinomatosis of colorectal origin - Incidence and current treatment strategies, *Annals of Surgery* 242 (2), pp. 212-222.

Levine, E. A., Blazer, D. G., Kim, M. K., Shen, P., Stewart, J. H., Guy, C., Hsu, D. S., 2012. Gene expression profiling of peritoneal metastases from appendiceal and colon cancer demonstrates unique biologic signatures and predicts patient outcomes, *Journal of the American College of Surgeons*, 214 (4), pp. 599 – 606.

Lungoci, C., Raus, I., Oniu, T., Moga, D., Stroia, N., Muntean, V., Petreus, D., Mironiuc, I. A., 2014. Assessment of temperature distribution in intraperitoneal chemohyperthermia, *International Conference on Advancements of Medicine and Health Care through Technology, IFMBE Proceeding,* 44, pp. 193–196, Cluj-Napoca.

Mikleš, D. J., Fikar, M., 2007. *Process modelling, identification, and control,* Springer. Verlag Berlin Heidelberg, Chapter 6 and 7.

Ogata, K., 2009. *Modern control engineering,* Prentice Hall. New Jersey, 5th edition.

Spratt, J. S., Adcock, R. A., Muskovin, M., Sherrill, W., Mckeown, J., 1980. Clinical delivery system for intraperitoneal hyperthermic chemotherapy, *Cancer Research*, 40 (2), pp. 256–260.

Stroia, N., Moga, D., Lungoci, C., Moga, R., and Petreus, D., 2014. Development of a hyperthermic intra-peritoneal chemotherapy equipment architecture based on the cyber-physical system paradigm, *Third International Workshop on Cyber Physical Systems*. Bucuresti.

Sugarbaker, P. H., 2005. *Technical handbook for the integration of cytoreductive surgery and perioperative intraperitoneal chemotherapy into the surgical management of gastrointestinal and gynecologic malignancy*, The Ludann Company Grand Rapids, Michigan, 4th edition.

Sugarbaker, P. H., Clarke, L., 2006. The approval process for hyperthermic intraoperative intraperitoneal chemotherapy, *European Journal of Surgical Oncology*, 32 (6), pp. 637-643.

Sugarbaker, P. H., 2012, Cytoreductive surgery plus hyperthermic perioperative chemotherapy for selected patients with peritoneal metastases from colorectal cancer: a new standard of care or an experimental approach?, *Gastroenterology Research and Practice,* 2012 ID:309417, 9 pages.

Szelitzky, T., Inoan, I., Dumitrache, D. C., 2011. Advantages of robust control for series load frequency controlled induction heating inverters, *Journal of Control Engineering and Applied Informatics*, 13 (1), pp. 62-68.