

## Discrete Time Sliding Mode Controller for Hyperthermia in Cancer Treatment

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**Abstract-** A Discrete time sliding mode controller based on Fast output sampling(DSMCFOS) via reduced order model is designed to manipulate the power levels of ultrasound transducer in the presence of blood perfusion variation to achieve controlled effective hyperthermia. A tumor layer surrounded by muscle layer is modeled by bio heat transfer equation and solved using finite difference method., Uncertainty in blood perfusion in tumor tissue model during the course of cancer treatment is considered ,to prove the robustness of sliding mode controller to parametric variation. Further since the algorithm is based on output feedback only the system output and past control inputs are used to implement the control law and state estimators are unnecessary. Designed fourth order controller is used to control 131 order system using aggregation matrix. Performance of the controller is assessed by framing a desired trajectory which meets the goals of on line hyperthermia feedback control system. The closed loop error norm and the open loop error norm for varying blood perfusion are validated. Simulations proved that the designed controller is effective and gives a much lower error norm numerically ranging from 0.3294 to 1.0043.

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### 1. Introduction

Cancer is a major threat to human life. Researchers are looking for improved cancer treatments over the existing methods of surgery, radiotherapy and chemotherapy. Hyperthermia the heating of cancerous tumours, can improve response rates when added as an adjuvant treatment to radiation therapy. Recent trials on human subject shows that in cervical cancer and recurrent lesions of malignant melanoma the response rate is 53% and 28% for patients who received radiation alone and the response rate has improved to 83% and 46% respectively for patients who received radiation in adjuvant with hyperthermia. The primary goal of an online hyperthermia controller is to achieve and maintain desired temperature  $\geq 43^{\circ}\text{C}$  within the tumor while limiting temperatures in normal tissues to safe levels  $\leq 41^{\circ}\text{C}$  (Mattingly et al 2000) .This objective must be met under the influence of variable blood flow rates that cool the tissue during the course of treatment, measurable disturbance such as displacement of tumor due to patient movement and pain, unknown disturbances as dynamic changes in blood perfusion , tissue properties and tissue ultrasound absorption rate leading to plant model mismatch (Dhiraj Arora et al 2002).

Previously many researchers have developed automatic temperature controllers for hyperthermia systems .Many control schemes in the range of basic PID (Lin et al 1990), Linear Quadratic Regulator controller (Hutchinson et al 1998), multipoint adaptive and even recursive control techniques (Jessi

et al 2006) were used to design the control system. Potocki & Tharp (1992) and Mattingly & Romer (2000) reduced the order of the hyperthermia system and designed optimal servo controller and inverse dynamics based control respectively for the reduced order model. Dhiraj Arora et al (2002) have formulated thermal treatment control problem as a problem of controlling thermal dose instead of controlling the temperature. This thermal dose is a single measure of treatment efficacy. Model Predictive Controller, minimum time thermal dose controller, constrained predictive thermal therapy controller (Dhiraj Arora et al 2002,2005,2007) are some of the dose controllers designed in recent past. Dose controllers may need either system linearization or strongly nonlinear control technique

Systems with sliding modes have proven to be very effective to control plants with uncertainties (Seung-Hi Lee and Chung Choo Chung 2003). This control technique works satisfactorily in the presence of external disturbances and parametric variations. The theory of sliding mode control is based on the concept of changing the structure of the controller in response to the changing states of the system in order to obtain the desired response (Utkin 1977). A high speed switching control action is used to switch between different structures and the trajectory of the system moves along the sliding surface. Once the states of the controlled system enter the sliding mode the system dynamics depends on the dynamics of the sliding surface and are independent of uncertainties

and disturbances (Bandhyopadhyay et al 2006, Inoue et al 2007).

Most of the design technique for sliding mode control is based on state feedback (Bandhyopadhyay et al 2007). Since all the system states may not be available for measurement in most practical cases, such controls are hard to implement. So sliding mode controllers are developed based on multirate output feedback controllers.

Sliding mode controller is specially appreciated for hyperthermia system because the temperature response of tumor tissues varies significantly with size, location, shape, stage of growth and proximity to vital organs. Also the blood perfusion changes as a function of time and tissue temperature. Long treatment time and changing blood perfusion during course of treatment lead to plant model mismatch

Although the existing controllers for hyperthermia are capable of satisfying the basic requirements of on line hyperthermia system they demand state estimators and does not guarantee robustness. During hyperthermia blood perfusion is the major variable that leads to parameter variation. So in the proposed method to compensate for the lack of robustness in the face of uncertainty in blood perfusion a Discrete Sliding Mode Controller using Fast Output Sampling (DSMCFOS) is designed. The key advantage of this approach is that it neither requires the states of the system for feedback nor an estimator to generate the control action (Saaj et al 2002). In FOS the output is measured at a faster rate and control is updated at a slow rate (Ezhilarasi et. al 2010). This feature makes the proposed control algorithm superior to state feedback based method. This study is a first effort towards incorporating sliding mode controller for hyperthermia system

**2. Material and Methods**

**Tumor & Ultrasonic Field Modeling**

A simple 1-D inhomogeneous tissue is modeled as a tumor layer surrounded by muscle layer on either side as in figure-1. Thermal response of tissue is modeled using the Penne’s bio heat transfer equation (Pennes. H.H 1948) and this provides useful predictions to estimate the temperature distribution in hyperthermia.

$$\rho C \frac{\partial T}{\partial t} = \nabla \cdot (k \nabla T) - W_b C_b (T - T_a) + Q_a \tag{1}$$

Arterial temperature  $T_a$  is assumed to be  $37^\circ\text{C}$  and  $Q_a$  is the power deposited in the ultrasonically heated tissue. The inhomogeneous tissue with tumor modeled in 1-D using Penne’s bio heat equation includes conduction effects, geometrical information about normal and diseased tissue. The parameters  $W_b$  in (1) represents the energy removed by conduction in the plane

perpendicular to the ultrasound axis. Table-1 summarize the thermal properties of human tissue

Table 1. Thermal properties of human tissue

|                                       | Symbol       | Muscle | Tumor |
|---------------------------------------|--------------|--------|-------|
| Thermal conductivity $W/(m^0C)$       | K            | 0.64   | 0.57  |
| Density $kg/ m^3$                     | $\rho$       | 1000   | 1000  |
| Specific heat capacity $J/(Kg^0C)$    | $C_1 \& C_2$ | 3500   | 4000  |
| Attenuation efficient $\alpha(N / m)$ | $\alpha$     | 18.5   | 20.5  |

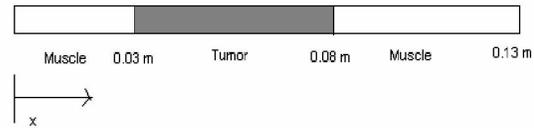


Figure 1. One dimensional inhomogeneous tissue

Thermal conductivity is assumed to be constant and ‘x’ is the depth of penetration inside the tissue. In this model ‘x’ varies from 0 to 13cm and the boundary condition are assumed to be  $T(0, t) = T_a$  and  $T(L, t) = T_a$ . The power deposition term  $Q_a$  is modelled as the energy deposited by single scanned focused ultrasound transducer and is given as

$$Q_i(x) = 2\alpha_i I(0) \left[ \frac{r}{r-x} \sin\left( \frac{\pi d^2(r-x)}{8\lambda x r} \right) \right]^2 e^{-\sum \alpha_i S_i} \tag{2}$$

Where  $Q_i(x)$ ,  $\alpha_i$  and  $S_i$  are energy deposition, attenuation co-efficient and penetration length for layer ‘i’. The transducer is positioned 17cm from the front edge of the tissue with  $r=25\text{cm}$ ,  $d=70\text{mm}$ ,  $\lambda=1\text{mm}$ . Where  $I(0)$  is the average intensity over the radiating surface ‘d’ is the diameter of the transducer ‘r’ is the radius of curvature and ‘x’ is the distance from the centre of the transducer

**State space formulation**

Finite difference method is used for solving the partial difference equation of bio heat transfer.

$$\frac{\partial T_{i,j}}{\partial t} = \frac{k}{\rho C (\Delta x)^2} T_{i+1,j} - \left[ \frac{2k}{\rho C (\Delta x)^2} + W_b C_b \right] T_{i,j} + \frac{k}{\rho C (\Delta x)^2} T_{i-1,j} + \frac{Q}{\rho C}$$

Assume  $T_{i,j} - T_a = T_{i,j}$  is the elevated temperature,

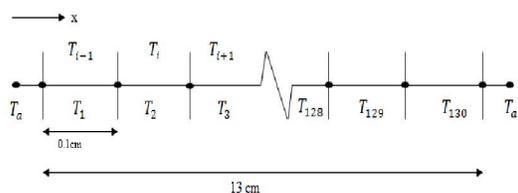


Figure 2 Finite difference nodes in tissue model



- To realize the state feedback gain F using output feedback, find the fictitious measurement matrix  $C_F$  using Equation

$$C_F(F, N) = (C_0 + D_0 F) (\Phi_\tau + \Gamma_\tau F)^{-1},$$

$$C_0 = \begin{bmatrix} c^T \\ c^T \Phi \\ \vdots \\ c^T \Phi^{N-1} \end{bmatrix}; D_0 = \begin{bmatrix} 0 \\ c^T \Gamma \\ \vdots \\ c^T \sum_{j=0}^{N-2} \Phi^j \Gamma \end{bmatrix}$$

- The state feedback gain F is converted to output feedback gain 'L' using the relation  $L = FC_F^{-1}$
- The control signal to be applied is given as  $u_k = Ly_k$ . this output feedback gain L is used to design the DSMCFOS.

Choose the parameters  $\varepsilon > 0$  and  $q > 0$ . By proper choice of parameters q and  $\varepsilon$ , the dynamic response of closed loop system can be improved. The key advantage of this approach is that it neither requires the states of the system for feedback nor an observer/estimator to generate the control action (Saaj et al 2002).

### Desired Trajectory

According to the control objective for hyperthermia system, temperature profile at each point in the tumor and on the normal tissue is an exponential function with time constant of  $\tau=0.008$  (Auxillia et al 2011). This function gives the desired trajectory for temperature rise at each point in tumor and in normal healthy tissues. For each case the error norm is calculated as the 2-norm of the difference between the desired trajectory and the achieved output trajectories.

$$\|e(t)\|_2 = \|y_{des}(t) - y_{out}(t)\| \tag{13}$$

$y_{des}$  - Desired trajectory. ;  $y_{out}$ - achieved output trajectory,  $e(t)$ - Error between the two temperature responses.

### 3. Results

#### System simulation

Space discretization of the model gives to 131 nodes including the boundary nodes. The power deposition will be maximum at the tumor nodes. Temperatures are measured using catheterized thermocouples in specific tumor and normal tissue locations. Perfusion conditions applied in simulation are given as tumor perfusion  $W_T$  and normal tissue perfusion  $W_N$ . The typical values  $W_T$  &  $W_N$  used in hyperthermia system modeling ranges from a lower extreme of 0.5  $kg/m^3sec$  to a higher extreme of 10  $kg/m^3sec$ . Four systems are considered with different combinations of  $W_T$  &  $W_N$  in this range. Open loop

response i.e. time temperature response of the four systems without controller is shown in figure-3.

Table-2 Different Perfusion Cases  $W_T$  -Tumor perfusion and  $W_N$ . Normal tissue perfusion

| Systems            | Blood Perfusion<br>( $kg/m^3s$ ) |
|--------------------|----------------------------------|
| System-1 $L_T L_N$ | $w_T=0.5, w_N=0.5$               |
| System-2 $L_T H_N$ | $w_T=0.5, w_N=10$                |
| System-3 $H_T L_N$ | $w_T=10, w_N=0.5$                |
| System-4 $H_T H_N$ | $w_T=10, w_N=10$                 |

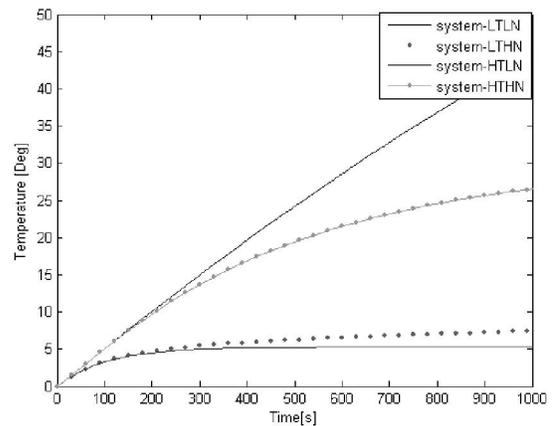


Figure-3 Time temperature response of tumor tissue model without controller

#### DSMCFOS applied to hyperthermia

The DSMCFOS is designed for the systems with  $\tau=12$  secs  $N = 10$ ;  $\Delta=1.2$  secs. Here  $\varepsilon$  and  $q$  are the controller parameters. Temperature response for all the four systems are obtained by fixing the tuning parameters as  $q = 0.3$ ;  $\varepsilon = 0.0007$ . The control thus obtained can be applied to the original higher order system using the aggregation matrix  $C_a$ . The designed DSMCFOS is put in loop with the simulated plant the closed loop trajectory of the resulting DSMCFOS and variation of the control signal 'u' with time 't' is graphically shown. From the simulations, it is seen that the DSMCFOS controller performed consistently well for different blood perfusion cases.

From the Figure 4(a)-7 (a) it is noticed that the measured temperature in each case reaches steady state approximately at 400 sec and there after it tracks the steady state without any fluctuations or overshoot. This makes the designed system suitable for online hyperthermia system.. The figures 4(b)-7(b) illustrates that the input powers needed were large initially and when the temperature reached the equilibrium point the input power compensated the

heat conduction to the surrounding tissue and after 400 sec it reached a constant value.

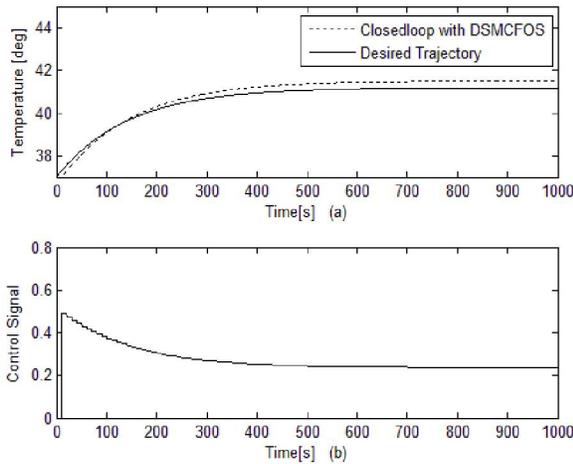


Figure-4 Temperature response for system-I using DSMCFOS (a) Closed loop temperature trajectory and desired trajectory (b) control effort

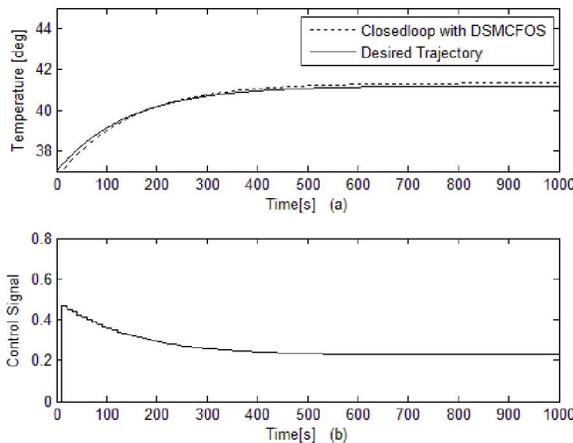


Figure-5 Temperature response for system-II using DSMCFOS (a) Closed loop temperature trajectory and desired trajectory (b) control effort

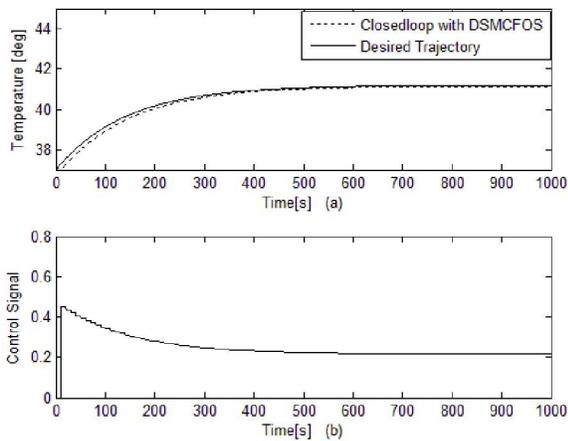


Figure-6 Temperature response for system-III using DSMCFOS (a) Closed loop temperature trajectory and desired trajectory (b) control effort

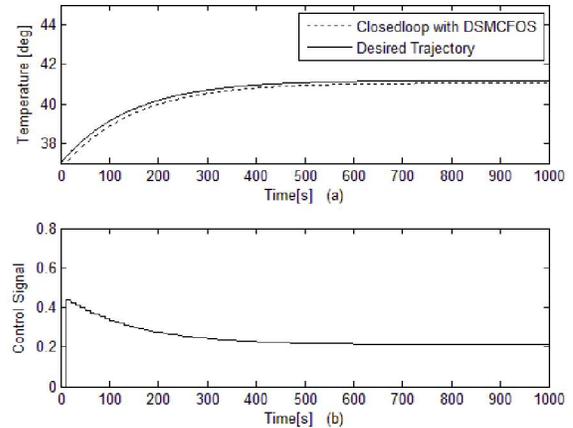


Figure-7 Temperature response for system-IV using DSMCFOS (a) Closed loop temperature trajectory and desired trajectory (b) control effort

**Closed loop system stability**

Stability of the closed loop system with DSMCFOS is given by analyzing the system behaviour in phase-plane (phase trajectory). It is found that the system stability is guaranteed if its phase trajectory in sliding mode is directed towards a stable equilibrium point. Figures-8 and 9 show the phase trajectories for closed loop system –I and system-II respectively using DSMCFOS .It is observed that the trajectory converges to the equilibrium point in finite time without circling around in phase-plane showing that the system reaches stability in finite time.

Table 3 Open loop and closed loop error norms with DSMCFOS for the four systems(measurement location at normal tissue)

| Systems               | Blood Perfusion $\text{kg}/(\text{m}^3\text{s})$ | Open loop error norm | Closed loop error norm with DSMCFOS |
|-----------------------|--|----------------------|-------------------------------------|
| System-1<br>$L_T L_N$ | $w_T=0.5,$<br>$w_N=0.5$                          | 109.00               | 0.7823                              |
| System-2<br>$L_T H_N$ | $w_T=0.5,$<br>$w_N=10$                           | 84.537               | 0.4389                              |
| System-3<br>$H_T L_N$ | $w_T=10,$<br>$w_N=0.5$                           | 114.100              | 0.3294                              |
| System-4<br>$H_T H_N$ | $w_T=10,$<br>$w_N=10$                            | 137.100              | 1.0043                              |

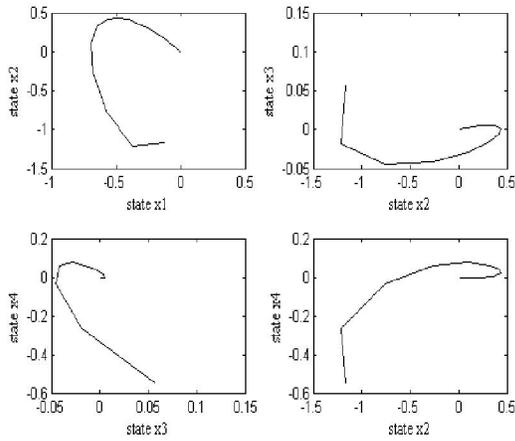


Figure-8 Phase trajectory of closed loop system –I using DSMCFOS

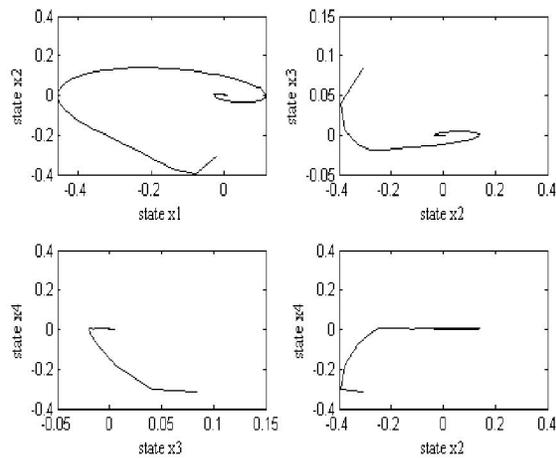


Figure-9 Phase trajectory of closed loop system –II using DSMCFOS

#### 4. Conclusion

A design methodology for hyperthermia treatment using discrete sliding mode controller using Fast Output Sampling via reduced order model is proposed and is substantiated by simulations. The DSMCFOS controller effectively adjusts the power level of the ultrasound transducer according to the blood perfusion to achieve controlled effective ultrasound hyperthermia. It is seen that the designed controller reduces the error norm drastically and the closed loop temperature trajectory tracks the desired trajectory for all perfusion cases. This gives clinical acceptance to hyperthermia treatment. Further, since the effect of state feedback gain is realized using an output feedback stability is guaranteed. Also the use

of observer is eliminated there by complexity of the system is reduced. Sliding mode controller designed for the reduced order model gives similar performance for the higher order system.

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