FEEDBACK CONTROL OF INTRACRANIAL PRESSURE USING MANNITOL

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A discrete-time model describing intracranial pressure (ICP) dynamics is extended to account for changes in blood osmolarity due to an i.v. injection of mannitol. It includes the effect of a blood osmolarity change on cerebrospinal fluid (CSF) formation and absorption. In order to maintain the ICP at a desired lowered level, a control algorithm is constructed. The controller is designed by minimizing a performance criterion, which consists of the mean squared error between the measured ICP and desired ICP, and the squared input. Minimizing the performance criterion specifies the controller. For on-line implementation, an approximately optimal controller is suggested. Simulation results show the feasibility of using this controller to regulate ICP.

Keywords — Intracranial pressure, ICP model, Intracranial hypertension, Automated drug delivery.

INTRODUCTION

An elevated intracranial pressure (ICP) level in patients represents a problem which can be deleterious to normal functioning of the central nervous system. One effective method of treatment in many cases is with drug therapy using mannitol (1,4,7,9,10), whereby it is desirable to keep the ICP within an acceptable range. A desired level of ICP can be maintained over a certain period by administering mannitol (i.v.) at an appropriate rate. This can be realized by means of a computerized control system. Given an appropriate mathematical model for the dynamics of ICP with the mannitol input, a control theoretical approach can give the drug regimens for maintaining the desired level of ICP. In the present study, a discrete-time model of ICP dynamics with a drug input is used to design a controller which regulates the mannitol injection rate in order to maintain a lowered ICP level.

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 MATHEMATICAL MODEL OF ICP

Based on the exponential pressure-volume relationship in the intracranial space, a continuous-time model of ICP dynamics in the absence of external inputs has been described in (5,6). The model describes the fluid balance in the intracranial space as the amount of CSF formed equal to the amount stored in the CSF space plus the amount that is absorbed into the dural venous sinuses; i.e.,

\[
I_f(t) = [\alpha P(t)]^{-1} \dot{P}(t) + \frac{P_{\text{net}}}{R}
\]  

(1)

where \(I_f\) is the CSF formation rate, \(P\) the ICP, \(V\) the intracranial volume, \(\alpha\) a parameter specified by the pressure-volume relationship, \(P_{\text{net}} = P(t) - P_d\) with \(P_d\) representing the dural sinus pressure, and \(R\) the resistance of CSF flow from the CSF space into the dural venous sinuses. Equation 1 does not contain an external input, such as a mannitol injection into the bloodstream.

The osmotic pressure difference between the CSF and blood is a significant factor in the ICP dynamics, causing considerable pressure changes within the CSF compartment. The driving force for fluid movement through a semi-permeable membrane is dependent upon the hydrostatic and osmotic pressure differences between the solutions on each side of the membrane. With mannitol in the blood circulation, the driving force, \(P_{\text{net}}\), across the arachnoid villi membrane can be represented as:

\[
P_{\text{net}} = \Delta P_h - \sigma_m \Delta \Pi_m \quad : \quad \Delta \Pi_m = -R_c T_c \Delta m
\]  

(2)

where \(\Delta P_h\) is the CSF hydrostatic pressure difference, \(\sigma_m\) the osmotic reflection coefficient for mannitol, \(\Delta \Pi_m\) the osmotic pressure difference between the CSF and the dural venous sinus, \(R_c\) the gas constant, \(T_c\) the absolute temperature in degrees Kelvin, and \(\Delta m\) the osmolarity change in the blood due to mannitol. The CSF hydrostatic pressure difference, \(\Delta P_h\), is described as the difference between the CSF pressure and the dural venous sinus pressure \((\Delta P_h = P - P_d)\). The value of \(\sigma_m\) is between 0 (for high permeabilities) and 1 (for low permeabilities).

Mannitol injection increases the blood osmolarity in the dural venous sinuses. This will tend to draw fluid from the CSF into the dural venous sinuses. The flow of fluid across the arachnoid villi can be expressed as \([P_{\text{net}} / R] = [\Delta P_h - \sigma_m \Delta \Pi_m] / R\), where \(\Delta P_h = [P(t) - P_d]\). This equation with Eq. 2 is substituted into Eq. 1 to obtain:

\[
I_f(t) = \frac{\dot{P}(t)}{\alpha P(t)} + \frac{P(t) - P_d}{R} + \frac{\sigma_m R_c T_c}{R} \Delta m(t)
\]  

(3)

Equation 3 is the modified ICP dynamical model describing the effect of the osmotic pressure changes due to mannitol in the blood.