Preliminary study of continuous glucose monitoring with a microdialysis technique and a null method — a numerical analysis

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Abstract—Monitoring of the subcutaneous tissue glucose concentration is an attractive method for continuous monitoring of the glucose concentration in diabetic patients. Several researchers have studied this, but no satisfactory method has been developed. We have proposed a new method, which can measure the glucose concentration of subcutaneous tissue continuously, even as the efficiency of membrane perfusion and sensor performance decline. Two reference solutions were prepared with concentrations higher and lower than the objective solution. They were perfused alternately for different ratios of perfusion times. The glucose concentration, after perfusing microdialysis, was detected and the trend of changes in the concentration was used to control the ratio of the two perfusion solutions. When the trend was a unity, the glucose concentration was calculated from the ratio of the two perfusion solutions. The numerical study was performed with a compartment model and a basic control theory. In simulation, the 90% response time to step change was approximately 7 min, which is fast enough when compared with the fluctuation of glucose in the electrolyte. This result suggested that this new system might be useful for continuous monitoring of the glucose concentration in subcutaneous tissue.

Key words: Glucose concentration; microdialysis; recovery rate; null method.

NOMENCLATURE

\[ Q \quad \text{perfusion rate} \]
\[ C_i \quad \text{concentration of reference solution} \]

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$C_d$ concentration in the outlet of the microdialysis probe
$C_1, C_2$ concentration in the microdialysis probe
$C_t$ concentration of the subcutaneous tissue
$k_{b1}, k_{b2}, k_t$ coefficient of both diffusive and convective resistance
$V_t$ volume of the subcutaneous tissue
$V_{b1}, V_{b2}$ volume of the microdialysis probe
$S$ surface of the membrane
$D$ diffusion coefficient
$\Delta r$ thickness of the membrane
$T_A, T_B$ perfusion time
$T$ time constant of the sensor
$v_o$ output of the sensor
$E_d$ recovery rate
$R$ ratio of the two perfusion times $T_A, T_B$

Subscripts

A reference solution of higher concentration than the objective solution
B reference solution of lower concentration than the objective solution

1. INTRODUCTION

The microdialysis technique is commonly used for long-term glucose monitoring [1–3]. In this method, a microdialysis probe is implanted in the subcutaneous tissue and dialysate is collected. The microdialysis probe has two concentric canulae. The tip of the outer cannula consists of a semipermeable membrane. When the probe is implanted in subcutaneous tissue and a saline solution flows through the tube, glucose and other substances flow into the tube through the membrane, because of the difference in concentration across the membrane. If the perfusion rate through the membrane (called the recovery rate) is known, the glucose concentration in the subcutaneous tissue can be monitored from the dialysate [4]. In such a system, sensor drift is troublesome and the recovery rate changes over time. Therefore, the system needs recalibration every few days.

To solve these problems, we attempted to develop a new microdialysis sampling system without the need for calibration. In this paper, we describe the numerical analysis of our new microdialysis sampling system.