

Article

Real-time PCR Machine System Modeling and a Systematic Approach for the Robust Design of a Real-time PCR-on-a-Chip System

Da-Sheng Lee

Department of Energy and Refrigerating Air Conditioning Engineering, National Taipei University of Technology, Taipei, Taiwan; E-Mail: fl1167@ntut.edu.tw; Tel.: +886-2-2771-2171 ext 3510; Fax: +886-2-2731-4919

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Abstract: Chip-based DNA quantification systems are widespread, and used in many point-of-care applications. However, instruments for such applications may not be maintained or calibrated regularly. Since machine reliability is a key issue for normal operation, this study presents a system model of the real-time Polymerase Chain Reaction (PCR) machine to analyze the instrument design through numerical experiments. Based on model analysis, a systematic approach was developed to lower the variation of DNA quantification and achieve a robust design for a real-time PCR-on-a-chip system. Accelerated life testing was adopted to evaluate the reliability of the chip prototype. According to the life test plan, this proposed real-time PCR-on-a-chip system was simulated to work continuously for over three years with similar reproducibility in DNA quantification. This not only shows the robustness of the lab-on-a-chip system, but also verifies the effectiveness of our systematic method for achieving a robust design.

Keywords: DNA quantification reliability; robust design; system identification model; real-time PCR machine; real-time PCR on-a-chip

1. Introduction

Wittwer *et al.* first began to develop real-time Polymerase Chain Reaction (PCR) machines in 1997 [1,2]. This type of instrument has an integrated fluorimeter to allow in-tube real-time analysis of DNA template samples. A rise in fluorescence of the signal of each cycle indicates amplification. The ability

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