

Article

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

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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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Table of Contents The Systematic Approach To Machine Design

1. Understanding the eBook The Systematic Approach To Machine Design
 - The Rise of Digital Reading The Systematic Approach To Machine Design
 - Advantages of eBooks Over Traditional Books
2. Identifying The Systematic Approach To Machine Design
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an The Systematic Approach To Machine Design
 - User-Friendly Interface
4. Exploring eBook Recommendations from The Systematic Approach To Machine Design

- Personalized Recommendations
 - The Systematic Approach To Machine Design User Reviews and Ratings
 - The Systematic Approach To Machine Design and Bestseller Lists
5. Accessing The Systematic Approach To Machine Design Free and Paid eBooks
 - The Systematic Approach To Machine Design Public Domain eBooks
 - The Systematic Approach To Machine Design eBook Subscription Services
 - The Systematic Approach To Machine Design Budget-Friendly Options
 6. Navigating The Systematic Approach To Machine Design eBook Formats
 - ePub, PDF, MOBI, and More
 - The Systematic Approach To Machine Design Compatibility with Devices
 - The Systematic Approach To Machine Design Enhanced eBook Features
 7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of The Systematic Approach To Machine Design
 - Highlighting and Note-Taking The Systematic Approach To Machine Design
 - Interactive Elements The Systematic Approach To Machine Design
 8. Staying Engaged with The Systematic Approach To Machine Design
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers The Systematic Approach To Machine Design
 9. Balancing eBooks and Physical Books The Systematic Approach To Machine Design
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection The Systematic Approach To Machine Design
 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
 11. Cultivating a Reading Routine The Systematic Approach To Machine Design
 - Setting Reading Goals The Systematic Approach To Machine Design
 - Carving Out Dedicated Reading Time
 12. Sourcing Reliable Information of The Systematic Approach To Machine Design

- Fact-Checking eBook Content of The Systematic Approach To Machine Design
 - Distinguishing Credible Sources
13. Promoting Lifelong Learning
- Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
14. Embracing eBook Trends
- Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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