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CAFFEINE MODEL IDENTIFICATION FOR VIGILANCE PERFORMANCE PREDICTION

by

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A Dissertation to the Faculty of
Old Dominion University in Partial Fulfillment of the
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ABSTRACT

CAFFEINE MODEL IDENTIFICATION FOR VIGILANCE PERFORMANCE PREDICTION

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Director: Dr. Jen-Kuang Huang

The pharmacodynamics and pharmacokinetics of caffeine have been well characterized. In this study, a caffeine dynamic model is developed to describe its pharmacodynamic effects on vigilance performance. Validated biomathematical models developed to address both individual and group fatigue and alertness in a non-laboratory setting represent a tremendous commercial opportunity. First, a test data set with caffeine effects isolated from circadian and homeostatic effects is created. Then a modeling approach for input and output effects is developed and different model structures for the caffeine effects are considered. Observer/Kalman filter Identification (OKID) algorithm is proposed and developed to identify the caffeine model from the created input/output data. The identified caffeine model is then tested to fit for the test data. In this caffeine model, five system parameters $[a_1, a_2, c_1, c_2, d_0]$ can be identified by using the proposed OKID algorithm. Identification of the individualized caffeine model shows that the first two coefficients $[a_1, a_2]$ have small variations for users of both low and high amounts of caffeine among all doses. The 100 mg model has a statistically higher caffeine response as compared to the response of the 200 mg or 300 mg models based on the individualized caffeine models identified from test data. The result also shows that users of both low and

high amounts of caffeine users have comparable responses based on the 100 mg model. However, the responses of the 200 mg or 300 mg models show that users of high amounts of caffeine have a statistically higher response to caffeine. In conclusion, the results suggest that the caffeine dosage and habitual usage do not have much impact on the individualized caffeine model dynamics, and the proposed individualized caffeine model can be modified by adding a dose factor to the input of the model to improve the prediction of the performance of other caffeine doses.

To
Migo♥

For
Phoebe♥

All Through
Jesus Christ♥

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Most of all, I thank God. God has manifested His presence in my life in so many ways that I would be doing a great injustice if I failed to say that He is the salient force behind all my success in life. Without Him, I am nothing. Through Him, all things are possible. All this was done in service to God. "When you go through the waters, I will be with you; and through the rivers, they will not go over you: when you go through the fire, you will not be burned; and the flame will have no power over" (Isaiah 43:2). Thank you, Lord Jesus.

TABLE OF CONTENTS

Page

LIST OF TABLE viii

LIST OF FIGURES ix

NOMENCLATURE xvii

Chapter

1. INTRODUCTION 1
   - 1.1 Background 1
   - 1.2 Objectives 2
   - 1.3 Dissertation Outlines 3

2. LITERATURE REVIEW 4
   - 2.1 Caffeine Effects 4
   - 2.2 Pharmacokinetics and Psychomotor Effects of Caffeine 7
   - 2.3 Techniques of Modeling 11

3. PREPARATION OF INPUT/OUTPUT DATA FOR CAFFEINE MODELING. 15

4. SYSTEM IDENTIFICATION METHOD 20
   - 4.1 Observer/Kalman Filter Identification (OKID) Algorithm 20
   - 4.2 Model Validation 30

5. CAFFEINE MODEL USING POPULATION AVERAGE DATA 31
   - 5.1 Identified Caffeine Model Using Population Average Data 31
   - 5.2 Input Noise Effect 37
   - 5.3 Optimal Caffeine Model Order 39
   - 5.4 State-space Model in Controllable Canonical Form 41
   - 5.5 Comparison of OKID and ARX Method 45

6. IDENTIFICATION OF INDIVIDUALIZED CAFFEINE MODEL 47
   - 6.1 Individualized Caffeine Model 47
   - 6.2 Effect of Caffeine Dosage on Individual Subject Performance 89
   - 6.3 Effect of Habitual Caffeine Usage on Individual Subject Performance 92

7. CAFFEINE MODEL PREDICTION 94

8. CONCLUSIONS 104

8.1 Overview 104
8.2 Areas for Future Work 105

REFERENCES 107

APPENDIXES
A. Single Caffeine Doses. 112
B. Repeated Trial Caffeine Doses 113

VITA 115

LIST OF TABLES

Table		Page
5.1	Noise Level Effect on Estimation Errors (RMSE) (2nd order)	38
5.2	Modeling Order Effect on Estimation Errors (RMSE) (5% noise)	40
5.3	Identified Model Coefficients from Population Averages	42
5.4	Model Coefficients from Population Averages	43
5.5	Dose Effect from Population Averages	43
5.6	Habitual Effect from Population Averages	44
5.7	Comparison of OKID and ARX Method	46
6.1	Individualized Caffeine Model Coefficients Identified for Gum 2 Subjects	83
6.2	Individualized Caffeine Model Coefficients Identified for Gum 3 Low-users	84
6.3	Individualized Caffeine Model Coefficients Identified for Gum 3 High-users	85
6.4	Individualized Caffeine Model Coefficients Statistics	86
6.5	Individualized Caffeine Model Coefficients Statistics for Dose Effect	87
6.6	Individualized Caffeine Model Coefficients Statistics for Habitual Effect	88

LIST OF FIGURES

Figure		Page
3.1	Population average performance measurements from the four test groups in the Gum 2 user data set	16
3.2	Differential effects between the Gum 2 user performance data and placebo data using population averages	17
3.3	Population average performance measurements from the four test groups in the Gum 3 low-user data set	17
3.4	Differential effects between the Gum 3 low-user performance data and placebo data using population averages	18
3.5	Population average performance measurements from the four test groups in the Gum 3 high-user data set	18
3.6	Differential effects between the Gum 3 high-user performance data and placebo data using population averages	19
3.7	Input model showing caffeine impulse inputs for Gum 3 200 mg high-user at times 0, 120 and 240 min. with additive white process noise	19
4.1	Values from Gum 2 using population averages	26
4.2	Singular values from Gum 3 low-user using population averages	27
4.3	Singular values from Gum 3 high-user using population averages	27
4.4	Procedure for Observer/Kalman filter identification (OKID) algorithm	29
5.1	Caffeine model developed for the differential effects between the Gum 2 50 mg and placebo cases using population averages	32
5.2	Caffeine model developed for the differential effects between the Gum 2 100 mg and placebo cases using population averages	33
5.3	Caffeine model developed for the differential effects between the Gum 2 200 mg and placebo cases using population averages	33
5.4	Caffeine model developed for the differential effects between the Gum 3 100 mg low-user and placebo cases using population averages	34

5.5 Caffeine model developed for the differential effects between the Gum 3 200 mg low-user and placebo cases using population averages 34

5.6 Caffeine model developed for the differential effects between the Gum 3 300 mg low-user and placebo cases using population averages 35

5.7 Caffeine model developed for the differential effects between the Gum 3 100 mg high-user and placebo cases using population averages 35

5.8 Caffeine model developed for the differential effects between the Gum 3 200 mg high-user and placebo cases using population averages 36

5.9 Caffeine model developed for the differential effects between the Gum 3 300 mg high-user and placebo cases using population averages 36

5.10 The best input noise pattern for Gum 3 200 mg high-user 38

5.11 Modeling errors (RMSE) as a function of number of additive input noise patterns used for running Gum 3 200 mg high-user data 39

5.12 Modeling errors (RMSE) as a function of estimated system order 40

5.13 Dose effect from population averages 44

5.14 Habitual effect from population averages 45

5.15 Estimation result using an ARX model (2^{nd} order Least-Squares Model for Gum 3 200 mg high-users from population averages) 46

6.1 Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 504 data and population averages placebo data 48

6.2 Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 506 data and population averages placebo data 48

6.3 Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 511 data and population averages placebo data 49

6.4 Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 513 data and population averages placebo data 49

6.5 Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 517 data and population averages placebo data 50

6.6 Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 521 data and population averages placebo data 50

6.7 Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 527 data and population averages placebo data 51

6.8 Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 535 data and population averages placebo data 51

6.9 Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 539 data and population averages placebo data 52

6.10 Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 507 data and population averages placebo data 52

6.11 Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 509 data and population averages placebo data 54

6.12 Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 524 data and population averages placebo data 54

6.13 Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 526 data and population averages placebo data 54

6.14 Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 529 data and population averages placebo data 54

6.15 Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 536 data and population averages placebo data 55

6.16 Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 537 data and population averages placebo data 55

6.17 Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 543 data and population averages placebo data 56

6.18 Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 545 data and population averages placebo data 56

6.19 Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 508 data and population averages placebo data 57

6.20 Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 510 data and population averages placebo data 57

6.21 Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 515 data and population averages placebo data 58

6.22 Individualized caffeine model developed for the differential effects between

Gum 2 200 mg subject 522 data and population averages placebo data 58

6.23 Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 528 data and population averages placebo data 59

6.24 Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 531 data and population averages placebo data 59

6.25 Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 533 data and population averages placebo data 60

6.26 Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 540 data and population averages placebo data 60

6.27 Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 541 data and population averages placebo data 61

6.28 Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 601 61

6.29 Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 603 62

6.30 Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 604 62

6.31 Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 609 63

6.32 Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 610 63

6.33 Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 611 64

6.34 Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 612 64

6.35 Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 616 65

6.36 Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 601 65

6.37 Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 603 66

6.38 Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 604 66

6.39 Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 609 67

6.40 Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 610 67

6.41 Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 611 68

6.42 Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 612 68

6.43 Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 616 69

6.44 Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 601 69

6.45 Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 603 70

6.46 Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 604 70

6.47 Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 609 71

6.48 Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 610 71

6.49 Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 611 72

6.50 Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 612 72

6.51 Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 616 73

6.52 Individualized caffeine model developed for the differential effects between Gum 3 100 mg high-user data and placebo data for subject 602 73

6.53 Individualized caffeine model developed for the differential effects between

Gum 3 100 mg high-user data and placebo data for subject 605 74

6.54 Individualized caffeine model developed for the differential effects between Gum 3 100 mg high-user data and placebo data for subject 608 74

6.55 Individualized caffeine model developed for the differential effects between Gum 3 100 mg high-user data and placebo data for subject 613 75

6.56 Individualized caffeine model developed for the differential effects between Gum 3 100 mg high-user data and placebo data for subject 614 75

6.57 Individualized caffeine model developed for the differential effects between Gum 3 100 mg high-user data and placebo data for subject 615 76

6.58 Individualized caffeine model developed for the differential effects between Gum 3 200 mg high-user data and placebo data for subject 602 76

6.59 Individualized caffeine model developed for the differential effects between Gum 3 200 mg high-user data and placebo data for subject 605 77

6.60 Individualized caffeine model developed for the differential effects between Gum 3 200 mg high-user data and placebo data for subject 608 77

6.61 Individualized caffeine model developed for the differential effects between Gum 3 200 mg high-user data and placebo data for subject 613 78

6.62 Individualized caffeine model developed for the differential effects between Gum 3 200 mg high-user data and placebo data for subject 614 78

6.63 Individualized caffeine model developed for the differential effects between Gum 3 200 mg high-user data and placebo data for subject 615 79

6.64 Individualized caffeine model developed for the differential effects between Gum 3 300 mg high-user data and placebo data for subject 602 79

6.65 Individualized caffeine model developed for the differential effects between Gum 3 300 mg high-user data and placebo data for subject 605 80

6.66 Individualized caffeine model developed for the differential effects between Gum 3 300 mg high-user data and placebo data for subject 608 80

6.67 Individualized caffeine model developed for the differential effects between Gum 3 300 mg high-user data and placebo data for subject 613 81

6.68 Individualized caffeine model developed for the differential effects between Gum 3 300 mg high-user data and placebo data for subject 614 81

6.69 Individualized caffeine model developed for the differential effects between Gum 3 300 mg high-user data and placebo data for subject 615 82

6.70 Individualized Caffeine Model Coefficients Statistics 86

6.71 Individualized Caffeine Model Coefficients Statistics for Dose Effect 87

6.72 Individualized Caffeine Model Coefficients Statistics for Habitual Effect 88

6.73 Individualized Performance Prediction Using One Caffeine Dose 90

6.74 Statistical response of individualized dose-dependent models to a single 100 mg caffeine input for eight Gum 3 low-users 91

6.75 Statistical response of individualized dose-dependent models to a single 100 mg caffeine input for six Gum 3 high-users 91

6.76 Statistical response of individualized 100 mg models to a single 100 mg input for eight low caffeine users as compared to six high caffeine users 92

6.77 Statistical response of individualized 200 mg models to a single 100 mg input for eight low caffeine users as compared to six high caffeine users 93

6.78 Statistical response of individualized 300 mg models to a single 100 mg input for eight low caffeine users as compared to six high caffeine users 93

7.1 Prediction of 100 mg caffeine effect using 200 mg model for high-users based on population average data 95

7.2 Prediction of 300 mg caffeine effect using 200 mg model for high-users based on population average data 95

7.3 Prediction of 100 mg caffeine effect using 200 mg model for low-users based on population average data 96

7.4 Prediction of 300 mg caffeine effect using 200 mg model for low-users based on population average data 96

7.5 Prediction of 50 mg caffeine effect using 100 mg model for Gum 2 based on population average data 97

7.6 Prediction of 200 mg caffeine effect using 100 mg model for Gum 2 based on population average data 97

7.7 Use of dose factor K to adjust input caffeine level for model prediction 99

7.8 Prediction of 100 mg caffeine effect using 200 mg model and an optimal dose factor for high-users based on population average data 99

7.9 Prediction of 300 mg caffeine effect using 200 mg model and an optimal dose factor for high-users based on population average data.....100

7.10 Prediction of 100 mg caffeine effect using 200 mg model and an optimal dose factor for low-users based on population average data.....100

7.11 Prediction of 300 mg caffeine effect using 200 mg model and an optimal dose factor for low-users based on population average data.....101

7.12 Prediction of 50 mg caffeine effect using 100 mg model and an optimal dose factor for Gum 2 on population average data.....101

7.13 Prediction of 200 mg caffeine effect using 100 mg model and an optimal dose factor for Gum 2 on population average data.....102

7.14 Optimal dose factor K vs. caffeine level for Gum 2 and Gum 3 based on population average data.....102

7.15 Optimal dose factor K vs. caffeine level for Gum 3 individualized Models.....103

NOMENCLATURE

$A(t)$	State matrix
a_1, a_2, c_1, c_2, d_0	Identified model coefficients
$B(t)$	Input matrix
$C(t)$	Output matrix
$D(t)$	Direct transmission matrix
$D, CB, CAB, \cdots, CA^{k-1}B$	System Markov Parameters
$D, C\overline{B}, C\overline{A}\overline{B}, \cdots, C\overline{A}^{(p-1)}\overline{B}$	Observer Markov parameters
e_i	Estimated value – test data at time step i
G	$n \times m$ arbitrary matrix chosen to make the matrix $\overline{\mathbf{A}}$ as stable as desired
H	Hankel matrix
K	Dose factor
k	K-th time step
m	Number of output
n	Number of state
p	P-th time step
r	Number of control output
$u(k) \in R^r$	Control input with dimension of r
$X(k) \in R^n$	State with dimension of n
$y(k) \in R^m$	Output with dimension of m

CHAPTER 1

INTRODUCTION

1.1 Background

Sleep deprivation and circadian misalignment occur frequently in military and labor operations, particularly during sustained operations and when multiple time zones are crossed during deployment. While sleep loss progresses, changes in performance and alertness occur in response to both increasing homeostatic sleep drive and circadian variation, resulting in an accumulation of performance deficits over time, superimposed on circadian modulation. Caffeine is a commonly used stimulant, known to alleviate the effects of sleep deprivation and fatigue. The pharmacodynamics and pharmacokinetics of caffeine have been well characterized. It is rapidly absorbed after oral dosing, and extensively metabolized. In military operations involving round-the-clock missions and travel across multiple time zones, biomathematical caffeine models of human performance have potential as tools for predicting, analyzing, and estimating the dose effect and habitual effect on the fatigue and performance of sleep-deprived soldiers. Validated biomathematical models developed to address both individual and group fatigue, sleepiness, and performance in non-laboratory settings represent a tremendous commercial opportunity. There is an articulated need to quantify the risks associated with worker fatigue, optimize schedules and procedures, and apply appropriate fatigue countermeasures to ensure acceptable levels of operational performance and safety.

* *Methods in Enzimology* of Academic Press was used as format model for this dissertation

Applications based on the tools in this research can help meet these needs, particularly in areas where human performance has important safety implications, such as military operations, air travel, emergency health care, shift work, etc. Therefore, it is essential to design biomathematical model development and system identification techniques, and develop a comprehensive set of caffeine model structures from both group and individual data sets. This approach allows a broad range of possible models to be analyzed and predicted. The data sets are from the U.S. Department of Defense, involving subjects repeating for one night total sleep deprivation conditions with caffeine doses administered through the night.

1.2 Objective

The objective of this research is to develop pharmacodynamic and forecasting models of caffeine administration as fatigue and performance countermeasures using a dynamic, individualized modeling framework. Models are developed that combine parameters such as dosage and administration timing with caffeine-related individual traits and habituation factors related to recent daily caffeine consumption. The research focuses on caffeine consumed in gum form. This modeling approach therefore starts with a comparative assessment of a range of model structures of various orders. Following testing, the most effective and parsimonious of the models is selected for subsequent integration with the Observer / Kalman Filter Identification (OKID) model. It is shown that the proposed individualized caffeine model can be modified by adding a dose factor to the input of the model to improve the prediction for the performance of other caffeine doses.

1.3 Dissertation Outlines

In this study, a caffeine dynamic model is developed to describe its pharmacodynamics effects on vigilance performance. First, a test data set with caffeine effects isolated from circadian and homeostatic effects is created. Then a modeling approach for input and output effects is developed and different model structures for the caffeine effects are considered. A system identification algorithm called Observer/Kalman filter Identification (OKID) is proposed and developed to identify the caffeine model from the created input/output data. The identified caffeine model is then tested to fit for the test data.

From the identified caffeine models, the effect of input noise and the model order on the modeling error is evaluated and an optimal model order is selected. After considering several model structures, an optimal caffeine model is recommended. Suitable caffeine parameters for individualization are identified. Based on the individualized models identified, the predicted caffeine performance for different caffeine dose and habitual caffeine usage is investigated. Finally, from the study of the group average and individualized caffeine-only test data, a state-space caffeine model in controllable canonical form is proposed for future study to merge into a two-process model with circadian and homeostatic effects.

CHAPTER 2

LITERATURE REVIEW

2.1 Caffeine Effects

It is well known that caffeine has effects on human behavior such as alertness, mood, mental performance and sleep. The effects of low doses (75 mg and 150 mg) of caffeine on mood and cognition in healthy people were evaluated, with minimal abstinence from caffeine of 1 hour. Improvements were obtained in cognition for attention, problem solving and delayed recall, but not immediate recall or working memory, but performance in the placebo condition was close to the maximum, giving little margin for improvement. For mood, there were statistically significant increases in clear-headedness, happiness and calmness and decreases in tenseness. These mood and performance-enhancing effects of caffeine cannot be seen as representing an alleviation of deficits induced by caffeine abstinence, because there was only minimal deprivation from caffeine (Warburton, 1995). In addition, the effects of caffeine on sleep inertia, which is the ubiquitous phenomenon of cognitive performance impairment, are that grogginess and tendency to return to sleep immediately after awakening. Caffeine was efficacious in overcoming sleep inertia. Caffeine's main mechanism of action on the central nervous system is antagonism of the adenosine receptor. Thus, increased adenosine in the brain upon awakening may be the cause of sleep inertia (Van Dongen et al., 2001). The ability of high doses of caffeine is assessed to reverse changes in alertness and mood produced by prolonged sleep deprivation (Penetar et al., 1993). In fact, there is little evidence

concerning the effects of caffeine in doses typical of one cup of tea. Durlach's study investigated the effect of 60 mg caffeine, consumed in either tea or hot water, on performance. The four beverages were created by crossing beverage identity (tea or hot water) and caffeine dose (0 or 60 mg). Significant speeding of reaction time by caffeine consumption was found in pattern recognition, delayed match to sample, and match to sample visual search. The effect on reaction time of 60 mg caffeine can be detected, and may be evident within minutes of consumption. Despite objective reports of immediate beneficial effects of consumption, most research has postponed measurement to coincide with peak plasma caffeine levels. The study was to investigate the effects of consuming a single cup of tea on a variety of cognitive tests (Durlach, 1998). A review of Lieberman's studies examined whether moderate doses of caffeine would reduce the adverse effects of sleep deprivation and exposure to severe environmental and operational stress on cognitive performance. Even in the most adverse circumstances, moderate doses of caffeine can improve cognitive function, including vigilance, learning, memory, and mood state. When cognitive performance is critical and must be maintained during exposure to severe stress, administration of caffeine may provide a significant advantage (Lieberman and Tharion, 2002). Smith's study suggests that the following effects on behavior of adult humans may occur when individuals consume moderate amounts of caffeine (Smith, 2002). Caffeine increases alertness and reduces fatigue. This may be especially important in low arousal situations (e.g. working at night). Caffeine improves performance on vigilance tasks and simple tasks that require sustained response. Again, these effects are often clearest when alertness is reduced, although there is evidence that benefits may still occur when the person is unimpaired. Effects on more complex tasks

are difficult to assess and probably involve interactions between the caffeine and other variables that increase alertness (e.g. personality and time of day). In contrast to the effects of caffeine consumption, withdrawal of caffeine has few effects on performance. There is often an increase in negative mood following withdrawal of caffeine, but such effects may largely reflect the expectancies of the volunteers and the failure to conduct "blind" studies. Regular caffeine usage appears to be beneficial, with higher users having better mental functioning. McLellan's study has demonstrated the effectiveness of caffeine for maintaining the performance of military tasks during a period of sleep deprivation. Vigilance during both a live-fire marksmanship task and in an urban operations environment was maintained at control levels when caffeine was ingested throughout the evening. The findings support the recommendation that during periods of unavoidable sleep loss the use of caffeine can extend the period of operational effectiveness during the conduct of military operations (McLellan et al., 2005).

Most people are very good at controlling their caffeine consumption to maximize the above positive effects. For example, the pattern of consumption over the day shows that caffeine is often consumed to increase alertness. Indeed, many people do not consume much caffeine later in the day since it is important not to be alert when one goes to sleep. In contrast to effects found from normal caffeine intake, there are reports that have demonstrated negative effects when very large amounts are given or when sensitive groups (e.g. patients with anxiety disorders) were studied. In this context caffeine has been shown to increase anxiety and impair sleep. There is also some evidence that fine motor control may be impaired as a function of the increase in anxiety. Overall, the global picture that emerges depends on whether one focuses on effects that are likely to

be present when caffeine is consumed in moderation by the majority of the population or on the effects found in extreme conditions. The evidence clearly shows that levels of caffeine consumed by most people have largely positive effects on behavior. Excessive consumption can lead to problems, especially in sensitive individuals.

The optimal dose of caffeine for sustaining performance has been determined during sleep loss with administration of multiple doses (Kamimori et al., 2005). When used to counteract the effects of sleep deprivation, multiple doses of caffeine are typically ingested across an extended period of time. The rapid delivery of caffeine in a chewing gum formulation can successfully maintain vigilance on a simple reaction time task using a multiple administration paradigm during a night without sleep. The ability of caffeine to improve or maintain alertness is directly dependent on the amount ingested, an individual's sensitivity to caffeine and on how fast it is ingested and absorbed into the body. The study findings demonstrate the efficacy of a multiple caffeine administration paradigm for maintenance of vigilance during simple reaction time performance through a night without sleep. Although any dose of caffeine was significantly better at countering the performance decrements observed in the placebo group, the 200-mg dose was most effective.

2.2 Pharmacokinetics and Psychomotor Effects of Caffeine

Both the pharmacokinetics and psychomotor effects of caffeine in humans have been investigated. Most research focused on the pharmacokinetics effect by finding the plasma caffeine level from the blood samples after the caffeine is administered. Robelin's study suggests that there is little net benefit to be gained from frequent caffeine use. At

the very least, it appears that the psychostimulant effects of caffeine cannot on their own account for the typical pattern of consumption of caffeine-containing drinks (Robelin and Rogers, 1998). Bovim's investigation was of the possible influence of caffeine upon motor steadiness performance in tests routinely used in neuropsychological testing. A significantly poorer motor steadiness performance was found after ingestion of 300 mg of caffeine as compared to a placebo (decaffeinated coffee). Both error time and error count were increased after caffeine consumption. Caffeine also tended to reduce maze coordination test performance. Hence, caffeine intake preferably should be avoided before neuropsychological testing of motor steadiness (Bovim et al., 1995). Furthermore, high-frequency low-dose caffeine administration is effective in countering the detrimental performance effects of extended wakefulness (Wyatt et al., 2004). Kaminmori studied body absorption of a single caffeine dose ingested in capsule form and as a gum to evaluate the rate and extent of absorption of three doses of caffeine from a gum versus a capsule formulation (Kamimori et al., 2002). The results indicate that the rate of drug absorption is significantly faster for the gum formulation. Although the bioavailabilities for 50, 100 and 200 mg gum groups are reported as 64, 74 and 77%, these bioavailabilities were based on 100% release of caffeine from the gum. However, data indicate that only 85% of the caffeine is released from the gum following 5 min of chewing (Novum, 2000). Based on an 85% dose, the mean bioavailabilities may be 75, 87 and 90% for the 50, 100 and 200 mg groups, respectively. It appears that for the 100 and 200 mg groups, the gum and capsule formulations provide a near comparable amount of caffeine to the systemic circulation. These findings suggest that both physical and mental performance deficits resulting from sleep loss or fatigue could be more quickly

reversed by caffeine administered in a chewing gum formulation compared with a capsule formulation.

Although the caffeine delivered through the gum formulation was intended to be absorbed through the oral mucosa, the use of four sticks of gum may have resulted in increased salivation (due to the large size of the gum cud) and a corresponding increase in the portion of the drug being swallowed with the saliva. The portion of caffeine swallowed in the saliva would be absorbed in the gastrointestinal tract, just like a capsule. In fact, we did observe multiple peaks in the plasma profiles of a number of subjects corresponding to multiple sites of absorption. Dual absorption sites could result in an immediate increase in plasma caffeine levels via absorption through the oral mucosa, followed by another peak corresponding to subsequent absorption in the gastrointestinal tract. However, this may have contributed to the high variability of the pharmacokinetic parameters, indicated by their high standard deviations. High variability could have also resulted from a parallel design of the study. Although a cross over study would have been the most elegant design, it was technically difficult. If the study was performed with a cross over design, there was an element of learning in the pharmacodynamic tasks that the subjects were asked to perform. Additionally, the subjects would alter their sleep pattern before their second study date based on their experience with the first study date. This would introduce bias and errors in the pharmacodynamic measurements. Caffeine improves performance and alertness in sleep deprived subjects, and in individuals who are required to work through the nadir of the circadian rhythm of alertness and performance in the early morning hours (e.g. medical and emergency personnel, long haul truckers, and shift workers) (Akerstedt and Ficca, 1997; Reyner and Horne, 1998).

Furthermore, the act of chewing gum itself has been shown to increase alertness in night shift workers (Hodoba, 1999).

Syed investigated body absorption of multiple caffeine doses ingested in gum (Syed et al., 2005). The rate of drug absorption from the gum formulation was significantly faster and may indicate absorption via the buccal mucosa. In addition, for the 100 and 200 mg groups, the gum and capsule formulations provide near comparable amounts of caffeine to the systemic circulation. These findings suggest that there may be an earlier onset of pharmacological effects of caffeine delivered in the gum formulation, which is advantageous in situations where the rapid reversal of alertness and performance deficits resulting from sleep loss is desirable. Their experimental results showed that the caffeine concentration can be described by a first order differential equation. A higher concentration of caffeine was found with higher intake dose level and had a nonlinear relationship with intake dose level.

Kaplan et al., 1997 also found that caffeine kinetics was nonlinear and the high-dose caffeine (250-500mg) produced less performance enhancement than the lower dose. Twelve healthy volunteers received an oral placebo, 250 mg of caffeine, and 500 mg of caffeine in a randomized, double-blind, single-dose crossover study. Caffeine kinetics was nonlinear, with clearance significantly reduced and elimination half-life prolonged at the 500 mg compared to the 250 mg dose. The lower dose of caffeine produced more favorable subjective effects than the higher dose (elation, peacefulness, pleasantness), whereas unpleasant effects (tension, nervousness, anxiety, excitement, irritability, nausea, palpitations, restlessness) following the 500 mg dose exceeded those experiments of the 250 mg dose. The lower dose of caffeine enhanced performance during the digit symbol

substitution test and the tapping speed test when compared to tests run with the placebo. High-dose caffeine produced less performance enhancement than the lower dose. The plasma concentration versus response relationship revealed concentration-dependent increases in anxiety and improvements in cognitive and motor performance at low to intermediate concentrations.

Both caffeine doses reduced electroencephalographic amplitude over the 4 Hz to 30 Hz spectrum, as well as in the alpha (8-11 Hz) and beta (12-30 Hz) ranges; however, effects were not dose-dependent. While favorable subjective and performance-enhancing stimulant effects occur at low to intermediate caffeine doses, the unfavorable subjective and somatic effects, as well as performance disruption, from high doses of caffeine may intrinsically limit the doses of caffeine used in the general population. Among the literatures surveyed, no suitable caffeine model has been found to represent the pharmacodynamics effects of caffeine on humans.

2.3 Techniques of Modeling

The process of using observed data to a mathematical model is fundamental in science and engineering. In the control area this process has been termed "System Identification" and the objective is then to find dynamical models (difference or differential equations) from observed input and output signals. Its basic features are, however, common with general model building processes in statistics and other sciences.

System Identification has been an active research area for more than thirty years. It has matured and many of the techniques have become standard tools in control and signal processing engineering. The approach is described Ljung (Ljung, 1987) and Soderstrom

(Soderstrom and Stoica, 1989). Over the past decades, there has been a significantly renewed interest in the area with topics like "unknown-but-bounded" disturbances (Schweppe, 1968) and (Milanese and Belforte, 1982), set membership techniques (Fogel, 1979; Norton, 1987) subspace techniques (Van, 1994), H_∞ identification (Parker and Bitmead, 1987; Helmicki, 1991), worst case analysis Guo and Khargonekar, 1992; Makila and Partington, 1991), as well as how to deal with unopened dynamics (Ninness, 1993). Ljung gave an overview and discussion of the basic steps of system identification (Ljung, 1994). The four main ingredients of the process that take us from observed data to a validated model are: (1) the data itself, (2) the set of candidate models, (3) the criterion of fit and (4) the validation procedure.

System Identification is used to develop an appropriate model of a dynamic system using observed data combined with prior knowledge of relationships between signals, input and output. It allows us to establish models for systems with very complex dynamics and/or systems with unknown physical parameter values. Juang built a bridge between the disciplines of system identification as applied to controls and to modal testing (Juang, 1994). The solid theoretical and methodological foundations from the control area should be combined with the extensive experimental knowledge from the modal testing field. When performing system identification experiments, we need to have the purpose of the identification in mind. In control problems, the final goal is to design control strategies for a particular system. The major benefit of system identification is the improvement of the analytical model of a system. System Identification is widely applied in many fields now, including ambient vibration testing and structural evaluation of an historic suspension footbridge (Gentile and Gallino, 2008), how stochastic sampling jitter

noise affects the result of system identification (Eng and Gustafsson, 2008), guided basis selection for reduced-order nonlinear response analysis (Rizzi and Przekop, 2008), the energy performance assessment of buildings and building components (Androutsopoulos *et al.*, 2008), dynamic fuel cell stack model for real-time simulation (Meiler *et al.*, 2008), modeling plant control strategies and their applications into a knowledge-based system (Marumo and Sebusang, 2008), input–output modeling with decomposed neuro-fuzzy ARX model (Golob and Tovornik, 2008), fast robust regression algorithms for problems with Toeplitz structure (Mastronardi and O'Leary, 2007), nonlinear system identification and control of chemical processes using fast orthogonal search (Eklund et al., 2007), FPGA implementation of a systems identification module based upon Hopfield networks (Atencia et al., 2007), A genetic approach to modeling fuzzy systems based on information granulation and successive generation-based evolution method (Park, 2007), dynamic characteristics of a curved cable-stayed bridge identified from strong motion records (Siringoringo and Fujino, 2007), isometric muscle contraction induced by repetitive peripheral magnetic stimulation (RPMS)—modeling and identification (Bernhardt et al., 2007) and system identification of photosensitiser uptake kinetics in photodynamic therapy (Bastogne et al., 2007).

A system identification algorithm called Observer/Kalman filter Identification (OKID) is proposed and developed to identify the caffeine model from the created input/output data. The Markov parameters can then be used for identification of a state space representation, with associated Kalman gain or observer gain, for the purpose of controller design. The algorithm is a non-recursive matrix version of two recursive algorithms developed in previous works for different purposes, and the relationship

between these other algorithms is developed. The new matrix formulation here gives insight into the existence and uniqueness of solutions of certain equations, and gives bounds on the proper choice of observer order. It is shown that if one uses data containing noise, and seeks the fastest possible deterministic observer, the deadbeat observer, one instead obtains the Kalman filter. It is important that the mathematical models obtained by means of system identification methods can be directly used for control system design purposes. This implies that linear models that take into account couplings between different motions should be determined. In fact, in such cases, linear control algorithms can be easily implemented and the effect of neglected dynamics can be minimized. An identification method that is potentially capable of coping with these requirements is observer/Kalman filter identification (OKID) that has proven to be numerically very efficient and robust with respect to measurement noise and even in the presence of mild nonlinearities. A number of successful applications of this method in the area of structural mechanics and aerospace engineering have been developed in recent years. The identified caffeine model is then tested to fit for the test data. Currently, observer/Kalman filter identification (OKID) algorithm applied to the identification of linear discrete-time multivariable models of an autonomous underwater vehicle (AUV) (Tiano et al., 2007), active vibration control of piezoelectric smart structures (Dong et al., 2006), low-order tuner for fault-tolerant control of a class of unknown nonlinear stochastic sampled-data systems (Chein et al. 2007), and to identify dynamic models of mechanical structures for comparison study of subspace to flexible structures (Abdelghani et al., 1998).

CHAPTER 3

PREPARATION OF INPUT/OUTPUT DATA FOR CAFFEINE MODELING

Our caffeine modeling begins with a black-box system identification approach as no suitable pharmacodynamics caffeine model has been found in the literature. Several laboratory-based test data sets have been provided by the Walter Reed Army Institute of Research for study. They include Gum 2 data sets with 0, 50, 100 and 200 mg caffeine doses and Gum 3 data sets with 0, 100, 200 and 300 mg caffeine doses for repeated high and low users of caffeine. It involved a total sleep deprivation condition with three caffeine boluses administered at 0, 120 and 240 minutes. All the data measured are for 1,000 ms lapses during a 10 minute PVT (Syed et al., 2005).

A test data set is created with the population averages for four conditions (see Figure 3.1) for Gum 2 data (0, 50, 100 and 200 mg), four conditions (see Figure 3.3) for Gum 3 low-user data (0, 100 and 200 and 300 mg), and four conditions (see Figure 3.5) for Gum 3 high-user data (0, 100, 200 and 300 mg). The measurements are conditioned for use as the output test data for system identification by subtracting each performance data for the caffeine case from the placebo data (0 mg). The created output data for the Gum 2 study is shown in Figure 3.2, for the Gum 3 low-user study in Figure 3.4, and for the Gum 3 high-user study in Figure 3.6. It is noted that a higher value of lapses shown in this caffeine-only data indicates higher alertness.

The caffeine input is structured as impulses proportional to the caffeine dose with additive white process noise. The impulse level selected is 5, 10, 20 and 30 for 50, 100, 200 and 300 mg caffeine doses, respectively. Figure 3.7 shows the input signal used for system identification for the Gum 3 200 mg high-user caffeine dose cases.

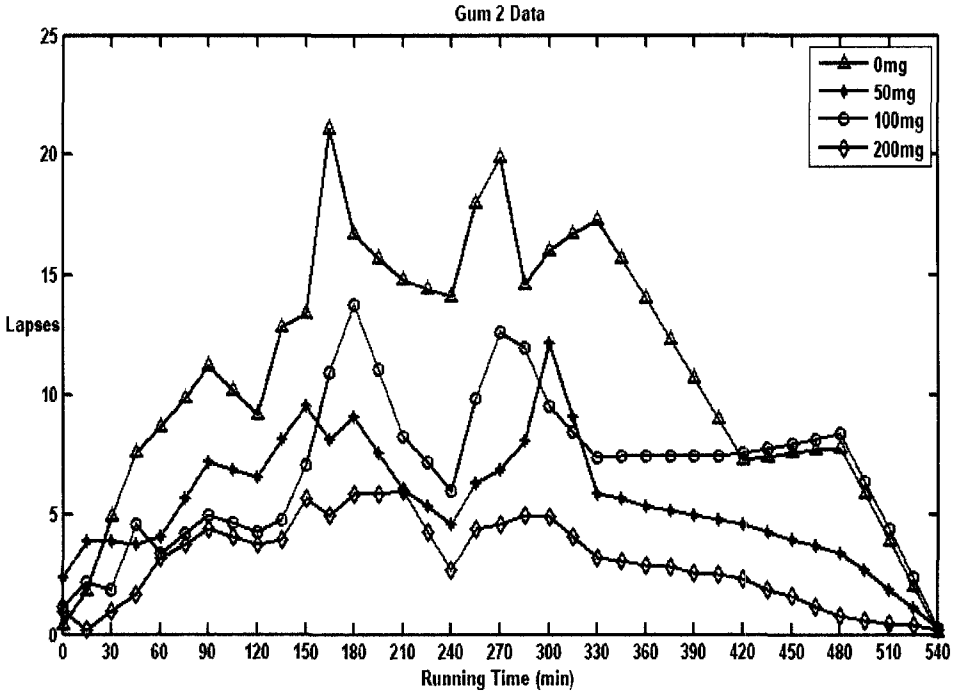

Figure 3.1: Population average performance measurements from the four test groups in the Gum 2 user data set.

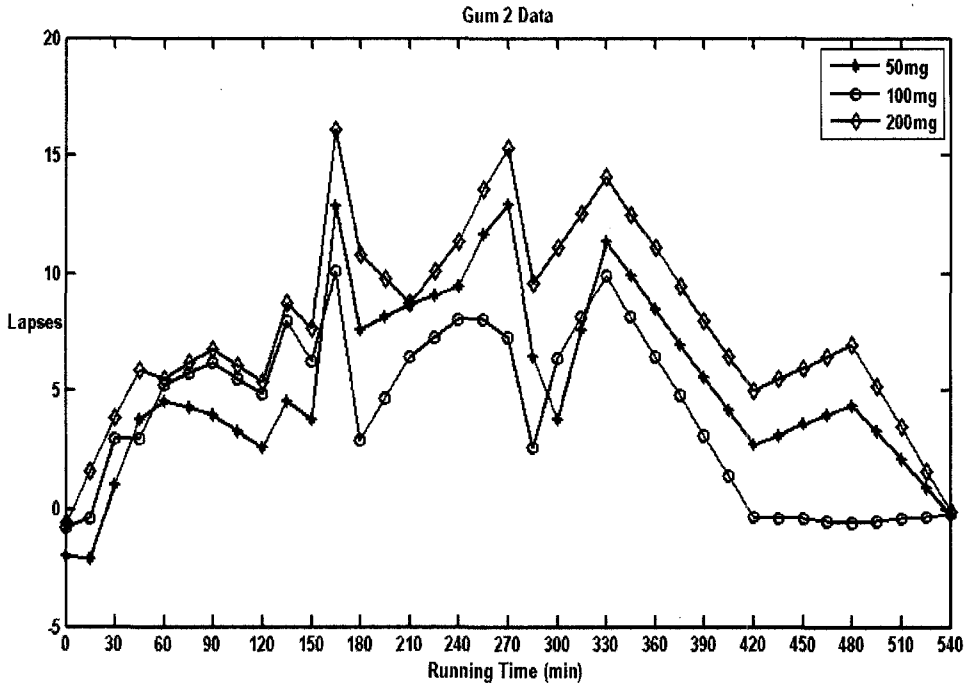

Figure 3.2: Differential effects between the Gum 2 user performance data and placebo data using population averages.

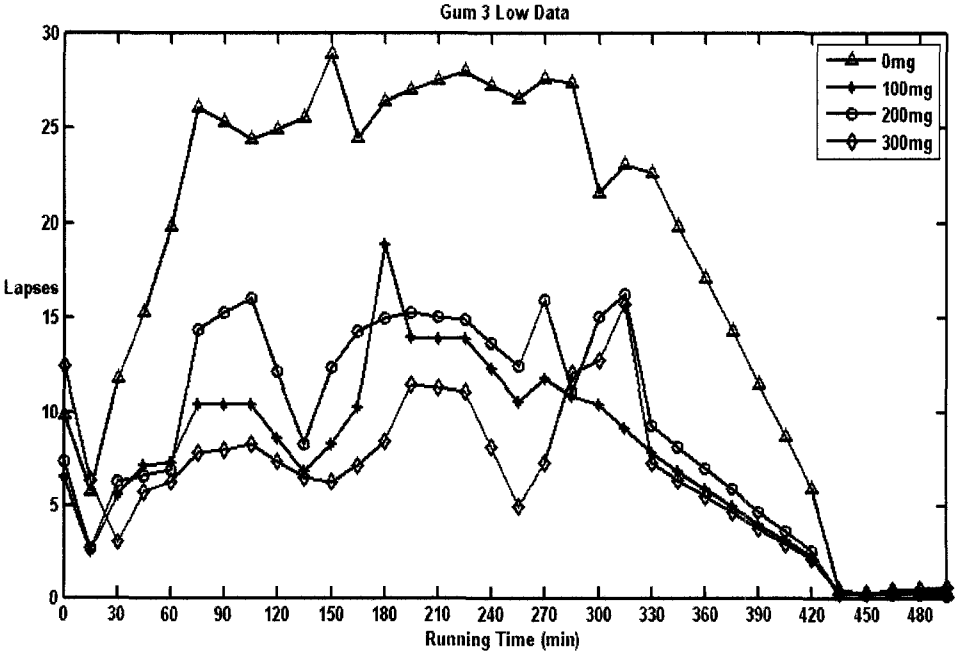

Figure 3.3: Population average performance measurements from the four test groups in the Gum 3 low-user data set.

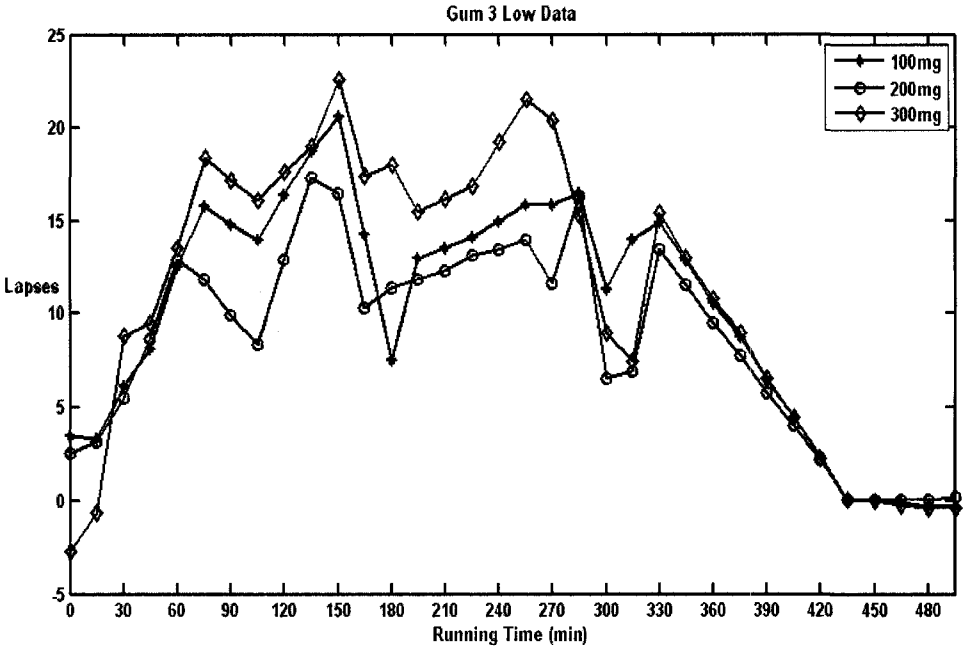

Figure 3.4: Differential effects between the Gum 3 low-user performance data and placebo data using population averages.

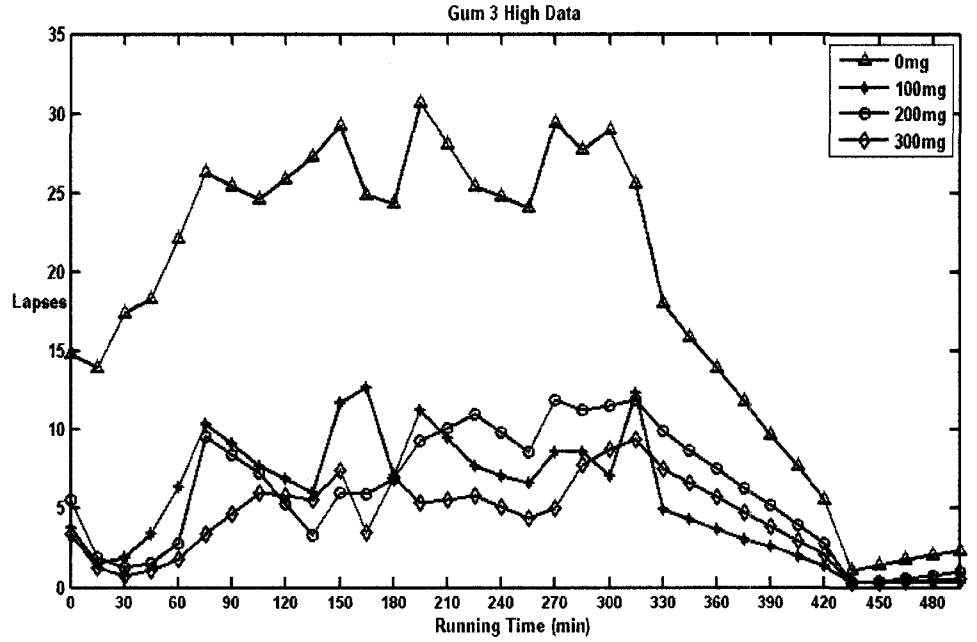

Figure 3.5: Population average performance measurements from the four test groups in the Gum 3 high-user data set.

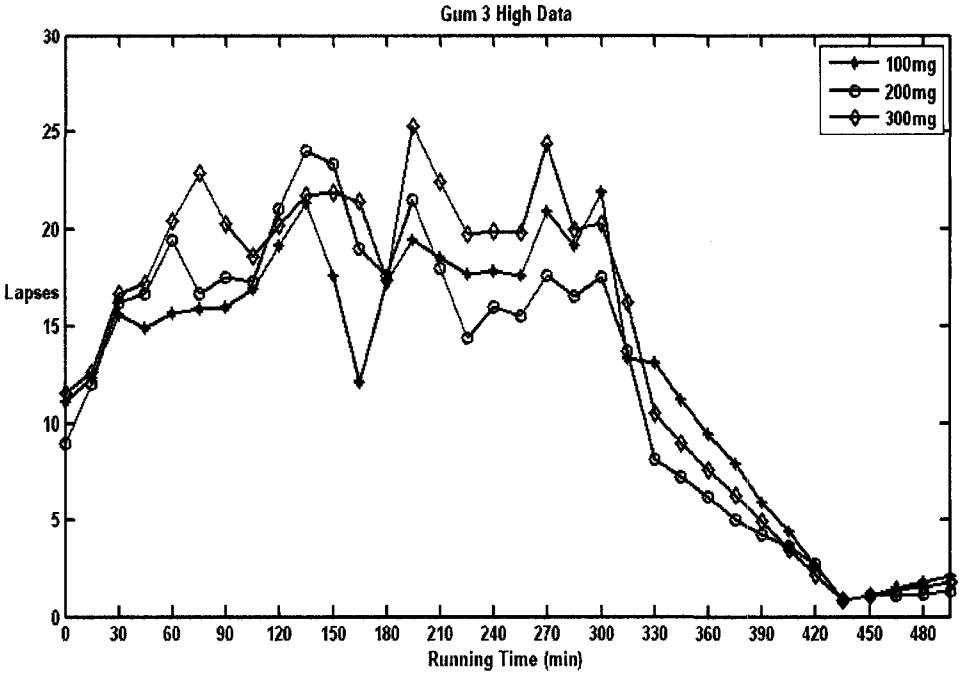

Figure 3.6: Differential effects between the Gum 3 high-user performance data and placebo data using population averages.

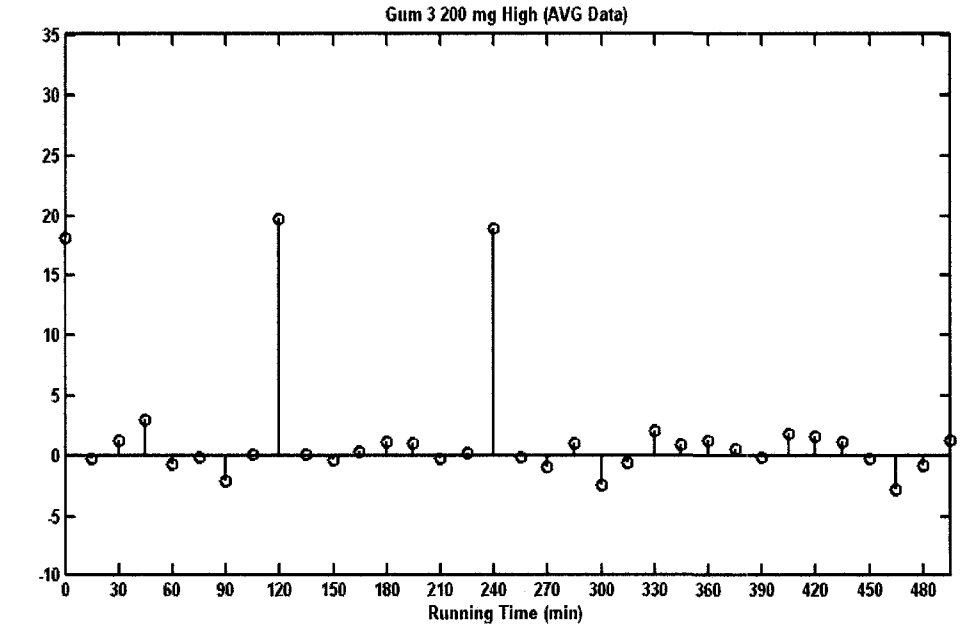

Figure 3.7: Input model showing caffeine impulse inputs for Gum 3 200 mg high-user at times 0, 120 and 240 min. with additive white process noise.

CHAPTER 4

SYSTEM IDENTIFICATION METHOD

4.1 Observer/Kalman Filter Identification (OKID) Algorithm

In the past decades, many system identification techniques have been developed and/or applied to identify a system model from test data. The Observer/Kalman filter identification (OKID) algorithm was first derived by Phan and then applied to many applications (Phan et al., 1992; Juang, 1994). The derivation of this algorithm is presented in this section.

A linear system can be represented by

$$\begin{aligned} \mathbf{X}(k+1) &= \mathbf{A}\mathbf{X}(k) + \mathbf{B}\mathbf{u}(k) \\ \mathbf{y}(k) &= \mathbf{C}\mathbf{X}(k) + \mathbf{D}\mathbf{u}(k) \end{aligned} \tag{4.1}$$

where $\mathbf{X}(k) \in R^n$, $\mathbf{y}(k) \in R^m$, $\mathbf{u}(k) \in R^r$ are state, output and control input with dimension of n, m, r respectively. From Eq. (4.1), the outputs $y(k)$ with zero initial state can be written in terms of the inputs $\mathbf{u}(i)$, $(i = 0, 1, 2, \cdots, k)$ as

$$\mathbf{y}(0) = \mathbf{D}\mathbf{u}(0)$$

$$\begin{aligned} \mathbf{y}(1) &= \mathbf{C}\mathbf{X}(1) + \mathbf{D}\mathbf{u}(1) \\ &= \mathbf{C}\mathbf{A}\mathbf{X}(0) + \mathbf{C}\mathbf{B}\mathbf{u}(0) + \mathbf{D}\mathbf{u}(1) \end{aligned}$$

$$
\begin{aligned}
\mathbf{y}(2) &= \mathbf{CX}(2) + \mathbf{Du}(2) \\
&= \mathbf{C}[\mathbf{AX}(1) + \mathbf{Bu}(1)] + \mathbf{Du}(2) \\
&= \mathbf{CA}^2\mathbf{X}(0) + \mathbf{CBu}(0) + \mathbf{CBu}(1) + \mathbf{Du}(2)
\end{aligned}
$$

$$
\begin{aligned}
\mathbf{y}(3) &= \mathbf{CX}(3) + \mathbf{Du}(3) \\
&= \mathbf{C}[\mathbf{AX}(2) + \mathbf{Bu}(2)] + \mathbf{Du}(3) \\
&= \mathbf{CA}[\mathbf{AX}(1) + \mathbf{Bu}(1)] + \mathbf{CBu}(2) + \mathbf{Du}(3) \\
&= \mathbf{CA}^2\mathbf{X}(1) + \mathbf{CABu}(1) + \mathbf{CBu}(2) + \mathbf{Du}(3) \\
&= \mathbf{CA}^2[\mathbf{AX}(0) + \mathbf{Bu}(0)] + \mathbf{CABu}(1) + \mathbf{CBu}(2) + \mathbf{Du}(3) \\
&= \mathbf{CA}^3\mathbf{X}(0) + \mathbf{CA}^2\mathbf{Bu}(0) + \mathbf{CABu}(1) + \mathbf{CBu}(2) + \mathbf{Du}(3)
\end{aligned}
$$

$$
\vdots
$$

$$
\mathbf{y}(k) = \mathbf{CA}^k\mathbf{X}(0) + \sum_{i=0}^{k-1} \mathbf{CA}^{k-1-i}\mathbf{Bu}(i) + \mathbf{Du}(k) \tag{4.2}
$$

When the initial state is zero, it can be written in the matrix form

$$
\overset{m\times l}{\mathbf{y}} = \underset{m\times rl}{\mathbf{Y}}\ \overset{rl\times l}{\mathbf{U}} \tag{4.3}
$$

where

$$
\mathbf{y} = \begin{bmatrix} \mathbf{y}(0) & \mathbf{y}(1) & \mathbf{y}(2) & \cdots & \mathbf{y}(l-1) \end{bmatrix}
$$

$$
\mathbf{Y} = \begin{bmatrix} \mathbf{D} & \mathbf{CB} & \mathbf{CAB} & \cdots & \mathbf{CA}^{l-2}\mathbf{B} \end{bmatrix}
$$

$$
\mathbf{U} = \begin{bmatrix}
\mathbf{u}(0) & \mathbf{u}(1) & \mathbf{u}(2) & \cdots & \mathbf{u}(l-1) \\
 & \mathbf{u}(0) & \mathbf{u}(1) & \cdots & \mathbf{u}(l-2) \\
 & & \mathbf{u}(0) & \cdots & \mathbf{u}(l-3) \\
 & & & \ddots & \vdots \\
 & & & & \mathbf{u}(0)
\end{bmatrix}
$$

The matrices $\mathbf{D}, \mathbf{CB}, \mathbf{CAB}, \cdots, \mathbf{CA}^{k-1}\mathbf{B}$ are called system Markov Parameters, and are commonly used as the basis to identify mathematical models for linear dynamic systems. A linear state-space model can be derived by forming a Hankel matrix using system Markov parameters.

For lightly damped systems, however, the slow decaying response may produce a large Hankel matrix, and long computation time. The OKID method solves this problem by adding an observer the system and placing desired eigenvalues, thus "forcing" the observer Markov parameters to be deadbeat. It adds and subtracts a term $\mathbf{Gy}(k)$ to the right-hand side of the state equation in Eq. (4.1), which yields

$$\begin{aligned}\mathbf{x}(k+1) &= \mathbf{Ax}(k) + \mathbf{Bu}(k) + \mathbf{Gy}(k) - \mathbf{Gy}(k) \\ &= (\mathbf{A}+\mathbf{GC})\mathbf{x}(k) + (\mathbf{B}+\mathbf{GD})\mathbf{u}(k) - \mathbf{Gy}(k)\end{aligned}$$

or $$\mathbf{x}(k+1) = \overline{\mathbf{A}}\mathbf{x}(k) + \overline{\mathbf{B}}\mathbf{v}(k) \tag{4.4}$$

where

$$\overline{\mathbf{A}} = \mathbf{A}+\mathbf{GC},\ \overline{\mathbf{B}} = [\mathbf{B}+\mathbf{GD} \quad -\mathbf{G}],\ \mathbf{v(k)} = \begin{bmatrix}\mathbf{u(k)} \\ \mathbf{y(k)}\end{bmatrix}$$

and G is an $n \times m$ arbitrary matrix chosen to make the matrix $\overline{\mathbf{A}}$ as stable as desired, i.e. places the eigenvalues of $\overline{\mathbf{A}}$ to any desired values. This ensures that $\mathbf{C}\overline{\mathbf{A}}^{k-1}\overline{\mathbf{B}} = 0$ for $k \geq p$.

From Eq. (4.4), the output $\mathbf{y}(k)$ with nonzero initial state can be written in terms of the inputs $\mathbf{v}(i) \quad (i = 0, 1, 2, \cdots, k)$ as

$$\mathbf{y}(0) = \mathbf{CX}(0) + \mathbf{Du}(0)$$
$$\mathbf{y}(1) = \mathbf{CX}(1) + \mathbf{Du}(1)$$
$$= \mathbf{C}\overline{\mathbf{A}}\mathbf{X}(0) + \mathbf{C}\overline{\mathbf{B}}\mathbf{v}(0) + \mathbf{Du}(1)$$

$$\mathbf{y}(2) = \mathbf{CX}(2) + \mathbf{Du}(2)$$
$$= \mathbf{C}[\overline{\mathbf{A}}\mathbf{X}(1) + \overline{\mathbf{B}}\mathbf{v}(1)] + \mathbf{Du}(2)$$
$$= \mathbf{C}\overline{\mathbf{A}}^2\mathbf{X}(0) + \mathbf{C}\overline{\mathbf{B}}\mathbf{v}(0) + \mathbf{C}\overline{\mathbf{B}}\mathbf{v}(1) + \mathbf{Du}(2)$$

$$\mathbf{y}(3) = \mathbf{CX}(3) + \mathbf{Dv}(3)$$
$$= \mathbf{C}[\overline{\mathbf{A}}\mathbf{X}(2) + \overline{\mathbf{B}}\mathbf{v}(2)] + \mathbf{Du}(3)$$
$$= \mathbf{C}\overline{\mathbf{A}}[\overline{\mathbf{A}}\mathbf{X}(1) + \overline{\mathbf{B}}\mathbf{v}(1)] + \mathbf{C}\overline{\mathbf{B}}\mathbf{v}(2) + \mathbf{Du}(3)$$
$$= \mathbf{C}\overline{\mathbf{A}}^2\mathbf{X}(1) + \mathbf{C}\overline{\mathbf{A}}\overline{\mathbf{B}}\mathbf{v}(1) + \mathbf{C}\overline{\mathbf{B}}\mathbf{v}(2) + \mathbf{Du}(3)$$
$$= \mathbf{C}\overline{\mathbf{A}}^2[\overline{\mathbf{A}}\mathbf{X}(0) + \overline{\mathbf{B}}\mathbf{v}(0)] + \mathbf{C}\overline{\mathbf{A}}\overline{\mathbf{B}}\mathbf{v}(1) + \mathbf{C}\overline{\mathbf{B}}\mathbf{v}(2) + \mathbf{Du}(3)$$
$$= \mathbf{C}\overline{\mathbf{A}}^3\mathbf{X}(0) + \mathbf{C}\overline{\mathbf{A}}^2\overline{\mathbf{B}}\mathbf{v}(0) + \mathbf{C}\overline{\mathbf{A}}\overline{\mathbf{B}}\mathbf{v}(1) + \mathbf{C}\overline{\mathbf{B}}\mathbf{v}(2) + \mathbf{Du}(3)$$

$$\vdots$$

$$\mathbf{y}(k) = \mathbf{C}\overline{\mathbf{A}}^k\mathbf{X}(0) + \sum_{i=0}^{k-1}\mathbf{C}\overline{\mathbf{A}}^{k-1-i}\overline{\mathbf{B}}\mathbf{v}(i) + \mathbf{Du}(k)$$

It can be written in the matrix form

$$\overline{\mathbf{y}} = init + \overline{\mathbf{Y}}\overline{\mathbf{V}} \tag{4.5}$$

where

$$\overline{\mathbf{y}} = [\mathbf{y}(p) \quad \mathbf{y}(p+1) \quad \cdots \quad \mathbf{y}(l-1)]$$
$$\overline{\mathbf{Y}} = [\mathbf{D} \quad \mathbf{C}\overline{\mathbf{B}} \quad \mathbf{C}\overline{\mathbf{A}}\overline{\mathbf{B}} \quad \cdots \quad \mathbf{C}\overline{\mathbf{A}}^{(p-1)}\overline{\mathbf{B}}]$$

$$\overline{\mathbf{V}} = \begin{bmatrix} \mathbf{u}(p) & \mathbf{u}(p+1) & \cdots & \mathbf{u}(l-1) \\ \mathbf{v}(p-1) & \mathbf{v}(p) & \cdots & \mathbf{v}(l-2) \\ \mathbf{v}(p-2) & \mathbf{v}(p-1) & \cdots & \mathbf{v}(l-3) \\ \vdots & \vdots & \vdots & \vdots \\ \mathbf{v}(0) & \mathbf{v}(1) & \cdots & \mathbf{v}(l-p-1) \end{bmatrix}$$

$$init = \left[\mathbf{C}\overline{\mathbf{A}}^{p}\mathbf{X}(0)\ \mathbf{C}\overline{\mathbf{A}}^{p+1}\mathbf{X}(0)\ \cdots\ \mathbf{C}\overline{\mathbf{A}}^{l-p-1}\mathbf{X}(0)\right]$$

The matrices $\mathbf{D},\mathbf{C}\overline{\mathbf{B}},\mathbf{C}\overline{\mathbf{A}}\overline{\mathbf{B}},\cdots,\mathbf{C}\overline{\mathbf{A}}^{(p-1)}\overline{\mathbf{B}}$ are called *observer Markov parameters.*

The first term in Eq. (4.5) represents the effect of the preceding p-1 time steps. When $\overline{\mathbf{A}}^{p}$ is sufficiently small and all the states in $\mathbf{x}$ are bounded, Eq. (4.5) can be approximated by neglecting the first term on the right-hand side,

$$\underset{m\times(l-p)}{\overline{\mathbf{y}}} = \underset{m\times[(m+r)p+r]}{\overline{\mathbf{Y}}} \overset{[(m+r)p+r]\times(l-p)}{\overline{\mathbf{V}}} \tag{4.6}$$

From Eq. (4.6), we can calculate the observer Markov parameters from the input/output data. The system Markov parameters can then be recovered from the observer Markov parameters $\overline{\mathbf{Y}}$ through partition of $\overline{\mathbf{Y}}$ as:

$$\overline{\mathbf{Y}}=[\mathbf{D}\ \ \mathbf{C}\overline{\mathbf{B}}\ \ \mathbf{C}\overline{\mathbf{A}}\overline{\mathbf{B}}\ \ \cdots\ \ \mathbf{C}\overline{\mathbf{A}}^{(p-1)}\overline{\mathbf{B}}]=[\overline{\mathbf{Y}}_0\ \ \overline{\mathbf{Y}}_1\ \ \overline{\mathbf{Y}}_2\ \ \cdots\ \ \overline{\mathbf{Y}}_p]$$

where the observer Markov parameters are

$$
\begin{aligned}
\overline{\mathbf{Y}}_0 &= \mathbf{D} \\
\overline{\mathbf{Y}}_k &= \mathbf{C}\overline{\mathbf{A}}^{(k-1)}\overline{\mathbf{B}} \\
&= [\mathbf{C}(\mathbf{A}+\mathbf{GC})^{k-1}(\mathbf{B}+\mathbf{GD}) \quad -\mathbf{C}(\mathbf{A}+\mathbf{GC})^{k-1}\mathbf{G}] \\
&= [\overline{\mathbf{Y}}_k^{(1)} \quad -\overline{\mathbf{Y}}_k^{(2)}]; \;\; k = 1,\, 2,\, 3, \cdots
\end{aligned}
\tag{4.7}
$$

The system Markov parameters can be calculated from the observer Markov parameters as

$$
\begin{aligned}
\mathbf{Y}_1 &= \mathbf{CB} = \mathbf{C}(\mathbf{B}+\mathbf{GD}) - (\mathbf{CG})\mathbf{D} \\
&= \overline{\mathbf{Y}}_1^{(1)} - \overline{\mathbf{Y}}_1^{(2)}\mathbf{D} \\
\mathbf{Y}_2 &= \mathbf{CAB} \\
&= \overline{\mathbf{Y}}_2^{(1)} - \overline{\mathbf{Y}}_1^{(2)}\mathbf{Y}_1 - \overline{\mathbf{Y}}_2^{(2)}\mathbf{D} \\
&\vdots
\end{aligned}
\tag{4.8}
$$

According to the above derivation, the general relationship between the system Markov parameters and the observer Markov parameters is

$$
\begin{aligned}
&\mathbf{D} = \mathbf{Y}_0 = \overline{\mathbf{Y}}_0 \\
&\mathbf{Y}_k = \mathbf{Y}_k^{(1)} - \sum_{i=1}^{k} \overline{\mathbf{Y}}_i^{(2)}\, \mathbf{Y}_{(k-i)} \qquad \text{for } k = 1, \cdots, p \\
&\mathbf{Y}_k = -\sum_{i=1}^{p} \overline{\mathbf{Y}}_i^{(2)}\, \mathbf{Y}_{(k-i)} \qquad \text{for } k = p+1,\; p+2 \cdots
\end{aligned}
\tag{4.9}
$$

or it can be written in system of equation as

$$
\begin{bmatrix}
\mathrm{I} & & & & \\
\overline{\mathbf{Y}}_1^{(2)} & \mathrm{I} & & & \\
\overline{\mathbf{Y}}_2^{(2)} & \overline{\mathbf{Y}}_1^{(2)} & \mathrm{I} & & \\
\vdots & \vdots & \vdots & \ddots & \\
\overline{\mathbf{Y}}_{p-1}^{(2)} & \overline{\mathbf{Y}}_{p-2}^{(2)} & \overline{\mathbf{Y}}_{p-3}^{(2)} & \cdots & \mathrm{I}
\end{bmatrix}
\begin{bmatrix}
\mathbf{Y}_1 \\ \mathbf{Y}_2 \\ \mathbf{Y}_3 \\ \vdots \\ \mathbf{Y}_p
\end{bmatrix}
=
\begin{bmatrix}
\mathbf{Y}_1^{(1)} - \mathbf{Y}_1^{(2)}\mathbf{D} \\
\mathbf{Y}_2^{(1)} - \mathbf{Y}_2^{(2)}\mathbf{D} \\
\mathbf{Y}_3^{(1)} - \mathbf{Y}_3^{(2)}\mathbf{D} \\
\vdots \\
\mathbf{Y}_p^{(1)} - \mathbf{Y}_p^{(2)}\mathbf{D}
\end{bmatrix}
$$

Finally, the desired discrete system realization $[\hat{\mathbf{A}}, \hat{\mathbf{B}}, \hat{\mathbf{C}}, \hat{\mathbf{D}}]$ can obtained from the system Markov parameters from singular value decomposition (SVD) of the Hankel matrix in Eq. (4.5) (see Figure 4.1 to 4.3).

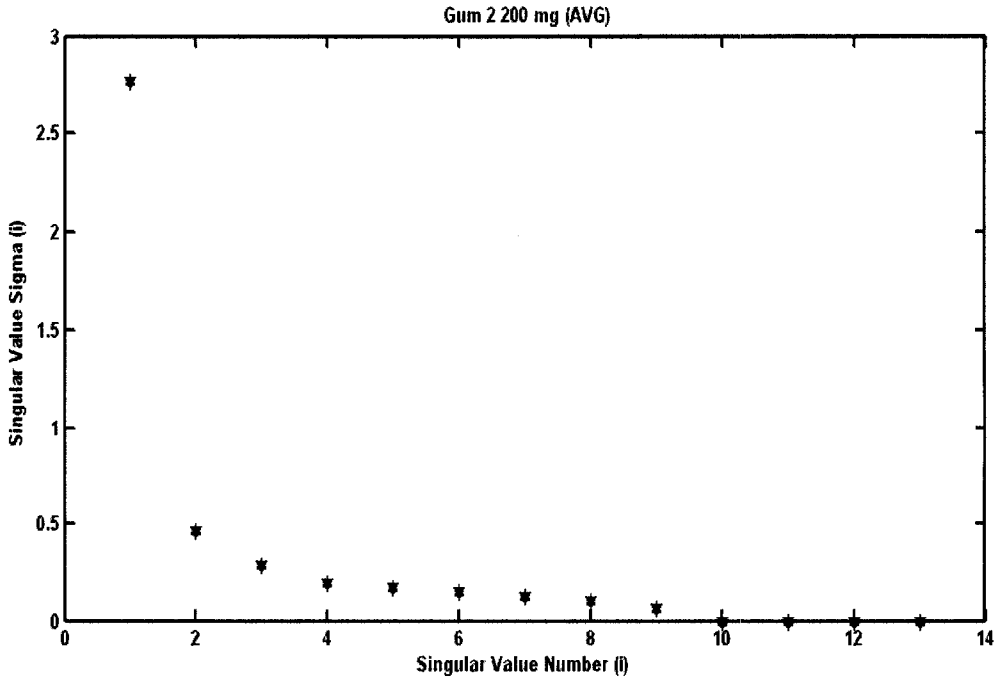

Figure 4.1: Singular values from Gum 2 using population averages.

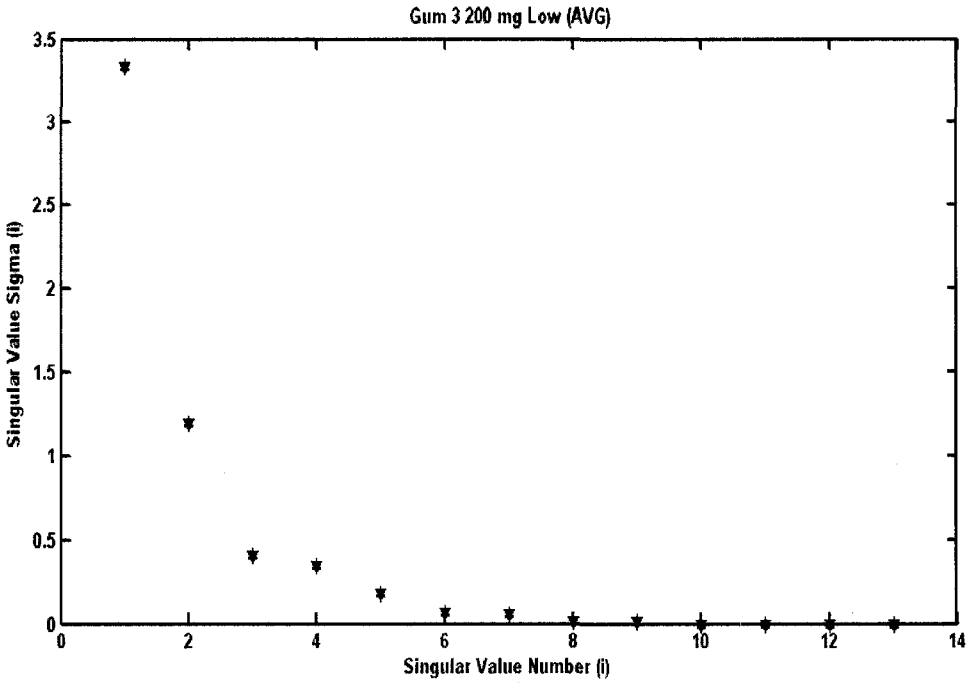

Figure 4.2: Singular values from Gum 3 low-user using population averages.

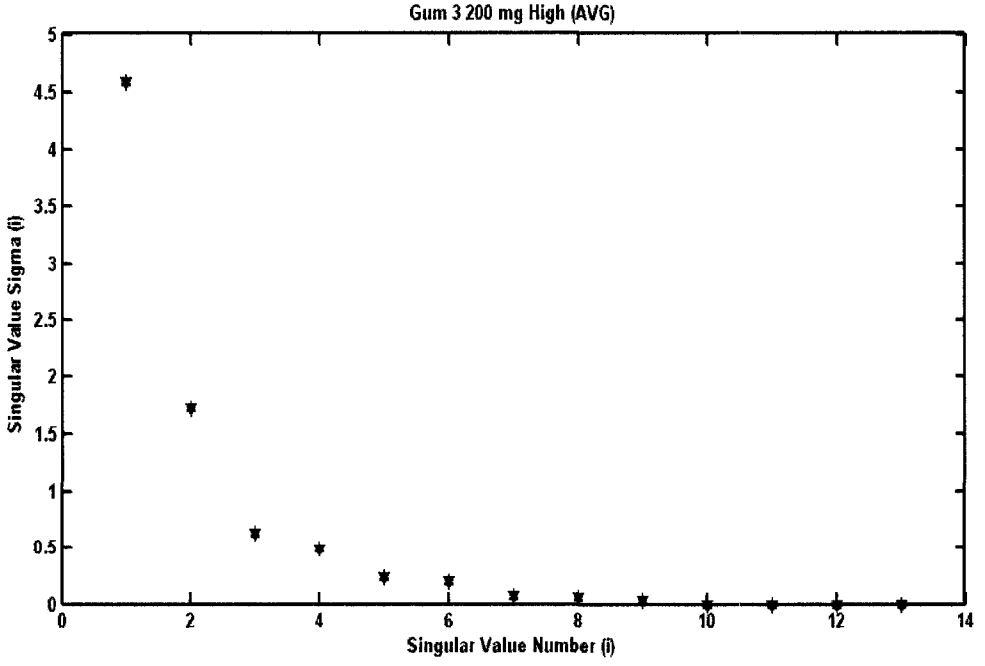

Figure 4.3: Singular values from Gum 3 high-user using population averages.

$$\mathbf{H}(k-1)=\begin{bmatrix} \mathbf{Y}_k & \mathbf{Y}_{k+1} & \cdots & \mathbf{Y}_{k+\beta-1} \\ \mathbf{Y}_{k+1} & \mathbf{Y}_{k+2} & \cdots & \mathbf{Y}_{k+\beta} \\ \vdots & \vdots & \ddots & \vdots \\ \mathbf{Y}_{k+\alpha-1} & \mathbf{Y}_{k+\alpha} & \cdots & \mathbf{Y}_{k+\alpha+\beta-2} \end{bmatrix} \tag{4.10}$$

$$\mathbf{H}(0)=\mathbf{R}_n\boldsymbol{\Sigma}\mathbf{S}_n$$

$$\hat{\mathbf{A}}=\boldsymbol{\Sigma}_n^{-1/2}\mathbf{R}_n^T\mathbf{H}(1)\mathbf{S}_n\boldsymbol{\Sigma}_n^{-1/2}$$

$$\begin{aligned} \hat{\mathbf{B}} &= \boldsymbol{\Sigma}_n^{1/2}\mathbf{S}_n^T\mathbf{E}_r \\ \hat{\mathbf{C}} &= \mathbf{E}_m^T\mathbf{R}_n\boldsymbol{\Sigma}_n^{1/2} \\ \hat{\mathbf{D}} &= \overline{\mathbf{Y}}_0 \end{aligned} \tag{4.11}$$

where $\mathbf{E}_m^T=[\mathbf{I}_m\ \mathbf{O}_m\cdots\mathbf{O}_m]$, $\mathbf{E}_r^T=[\mathbf{I}_r\ \mathbf{O}_r\cdots\mathbf{O}_r]$.

The estimation system can be represented by

$$\begin{aligned} \mathbf{X}(k+1) &= \hat{\mathbf{A}}\mathbf{X}(k)+\hat{\mathbf{B}}\mathbf{u}(k) \\ \mathbf{y}(k) &= \hat{\mathbf{C}}\mathbf{X}(k)+\hat{\mathbf{D}}\mathbf{u}(k) \end{aligned} \tag{4.12}$$

The caffeine model can be identified by using the OKID algorithm with the following steps:

a. Obtain input/output time histories data.

b. Calculate Observer Markov parameters.

c. Calculate System Markov parameters.

d. Choose system order after finding singular values of the system Hankel matrix.

e. Find system matrices A, B, C, D.

f. Derive system parameters.

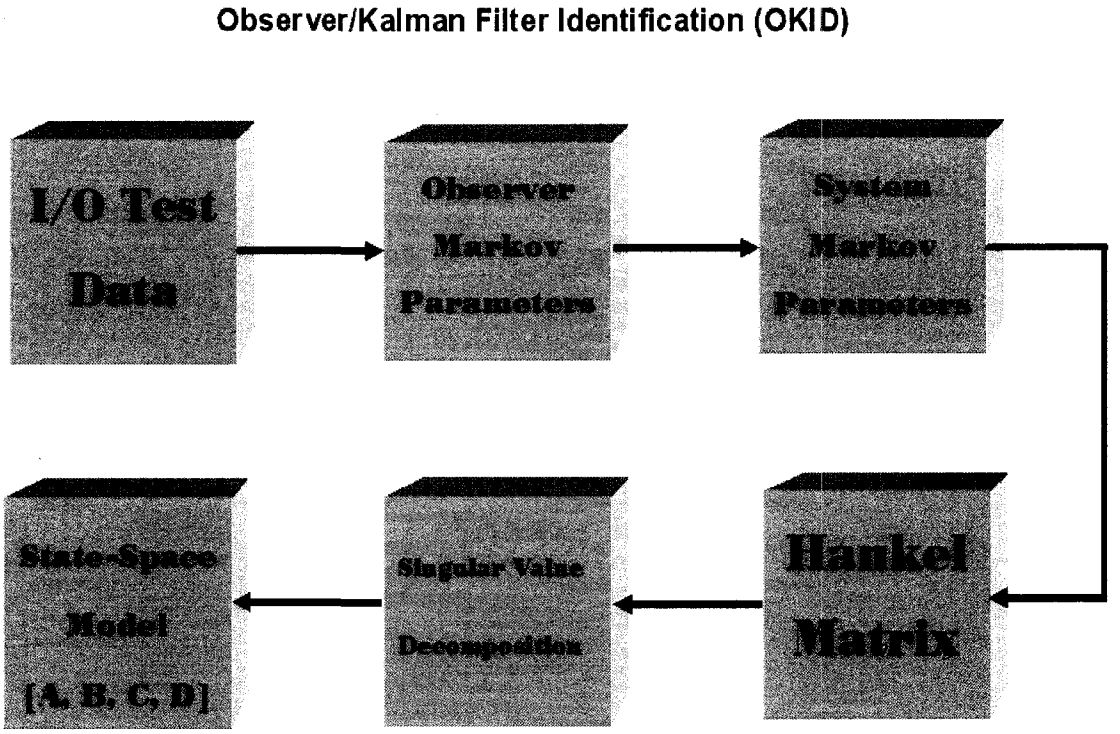

Figure 4.4: Procedure for Observer/Kalman filter identification (OKID) algorithm

4.2 Model Validation

The multi-pulse input signal without additive white process noise is used as the input to the identified model for output estimation. The accuracy of the identified model is validated by calculating the root mean squared error (RMSE) of the estimated output signal:

$$RMSE = \left(\frac{1}{n} \sum_{i=1}^{n} e_i^2 \right)^{1/2}, \quad e_i = \text{estimated value} - \text{test data at time step } i \qquad (4.13)$$

CHAPTER 5

CAFFEINE MODEL USING POPULATION AVERAGE DATA

The OKID algorithm is used to identify the caffeine model for the Gum 2 and Gum 3 population average data. In each case, several sets of white process noise are added to the multi-pulse input. From OKID, a second order caffeine model is identified for each set of input noise. After model validation, the model with the least modeling error is selected as the identified model. From the identified caffeine model, the effect of input noise and model order on the modeling error is evaluated and an optimal model order is selected. After considering several model structures, an optimal caffeine model is recommended.

5.1 Identified Caffeine Model Using Population Average Data

As a demonstration, this approach applied to the Gum 3 200 mg high-user case yields a caffeine effects model of

$$x(k+1) = Ax(k) + Bu(k), \quad y(k) = Cx(k) + Du(k)$$

$$A = \begin{bmatrix} 0.890 & -0.187 \\ 0.1870 & 0.863 \end{bmatrix}, \; B = \begin{bmatrix} -0.960 \\ 0.541 \end{bmatrix}, \; C = \begin{bmatrix} -0.960 & -0.541 \end{bmatrix}, \; D = 0.306$$

Its equivalent ARX model is:

$$y(k) + a_1 y(k-1) + a_2 y(k-2) = b_0 u(k) + b_1 u(k-1) + b_2 u(k-2)$$

$a_1 = -1.753, a_2 = 0.803, b_0 = 0.306, b_1 = 0.093, b_2 = -0.096$

Figures 5.1 to 5.9 show the results of caffeine model developed for Gum 2 and Gum 3 population averages. The input impulse level plotted in the figures is scaled down from the actual level used in the simulations by a factor of 10.

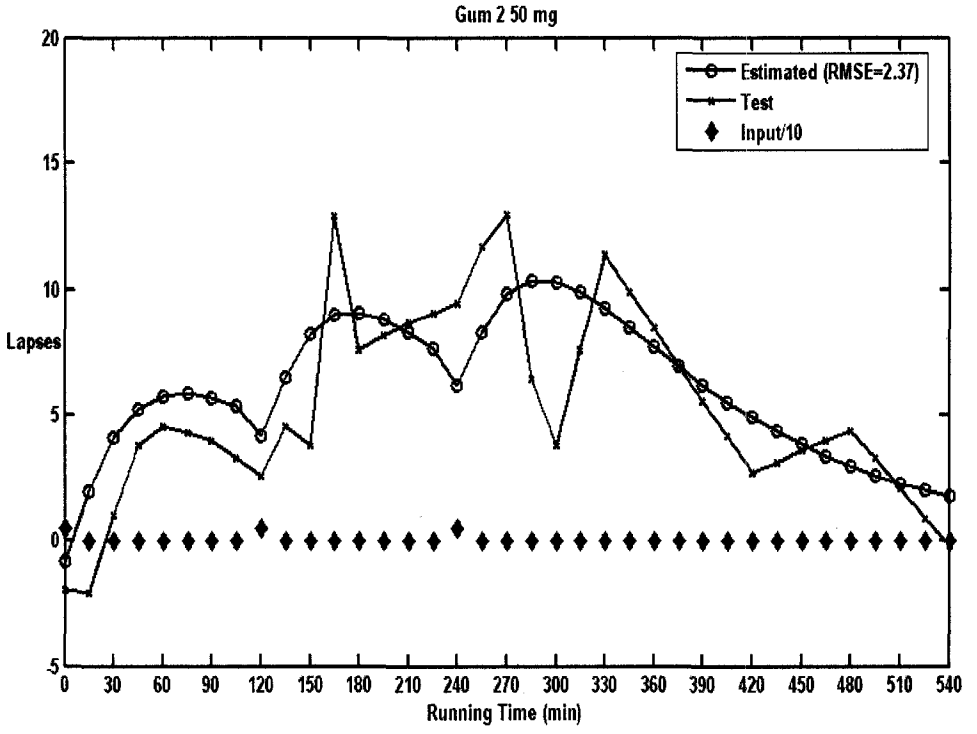

Figure 5.1: Caffeine model developed for the differential effects between the Gum 2 50 mg and placebo cases using population averages.

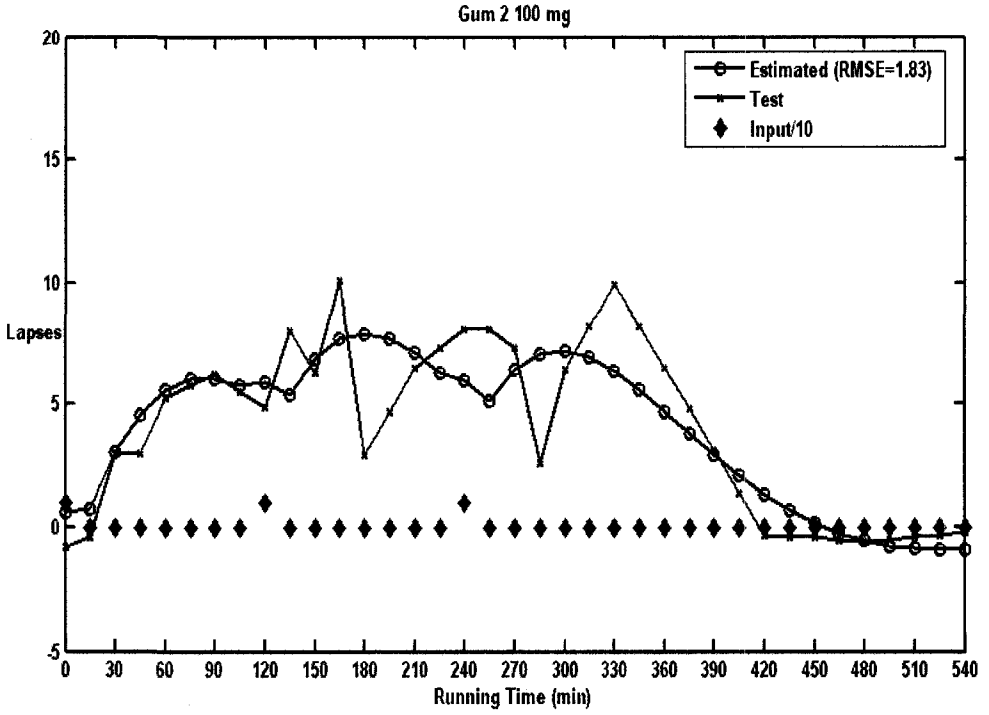

Figure 5.2: Caffeine model developed for the differential effects between the Gum 2 100 mg and placebo cases using population averages.

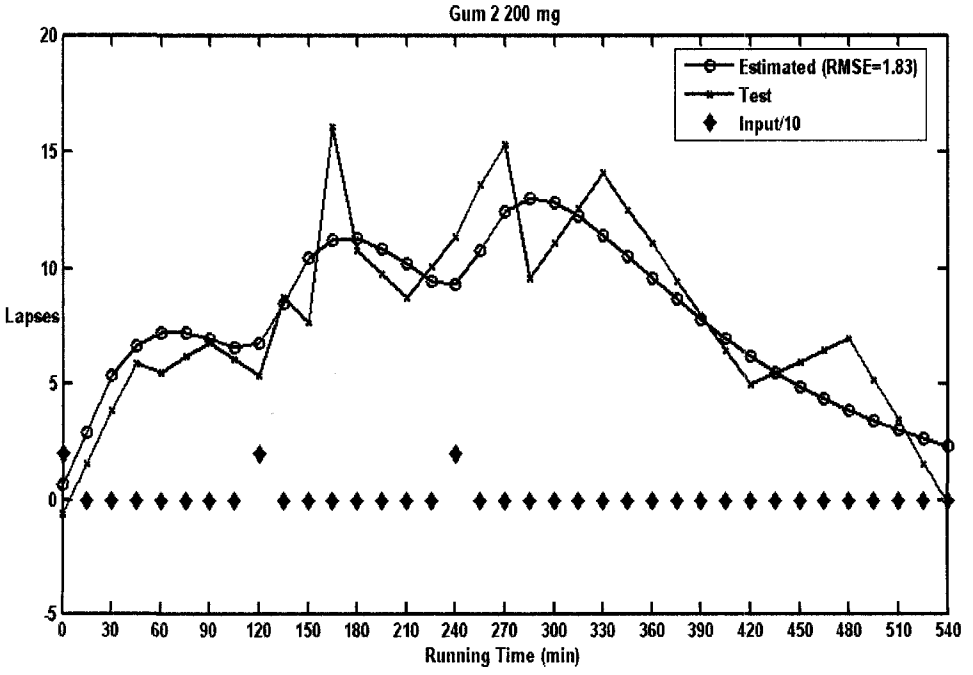

Figure 5.3: Caffeine model developed for the differential effects between the Gum 2 200 mg and placebo cases using population averages.

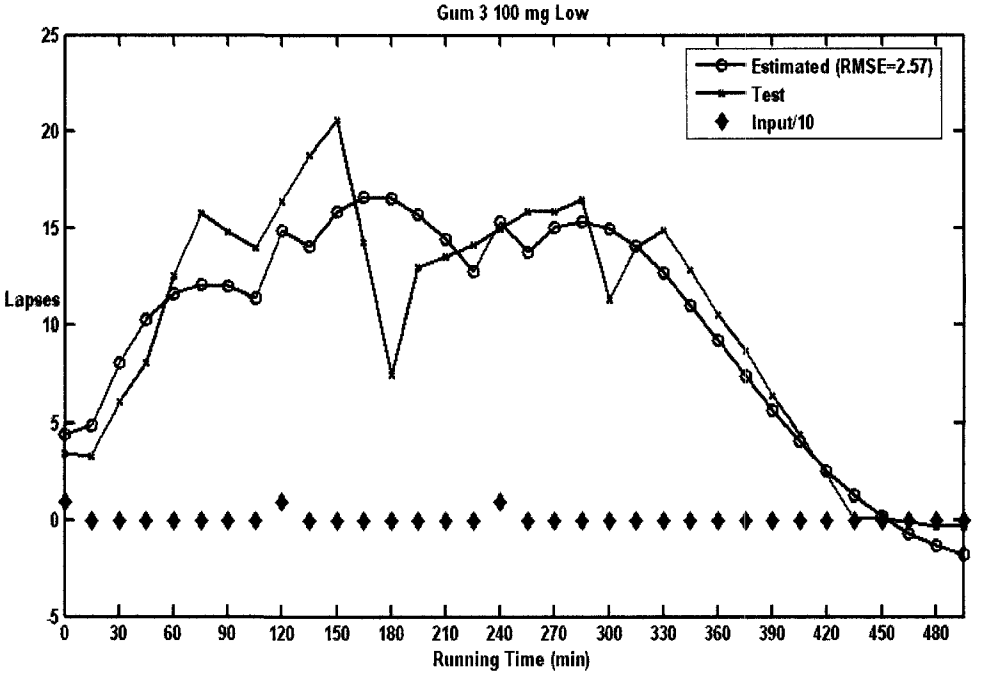

Figure 5.4: Caffeine model developed for the differential effects between the Gum 3 100 mg low-user and placebo cases using population averages.

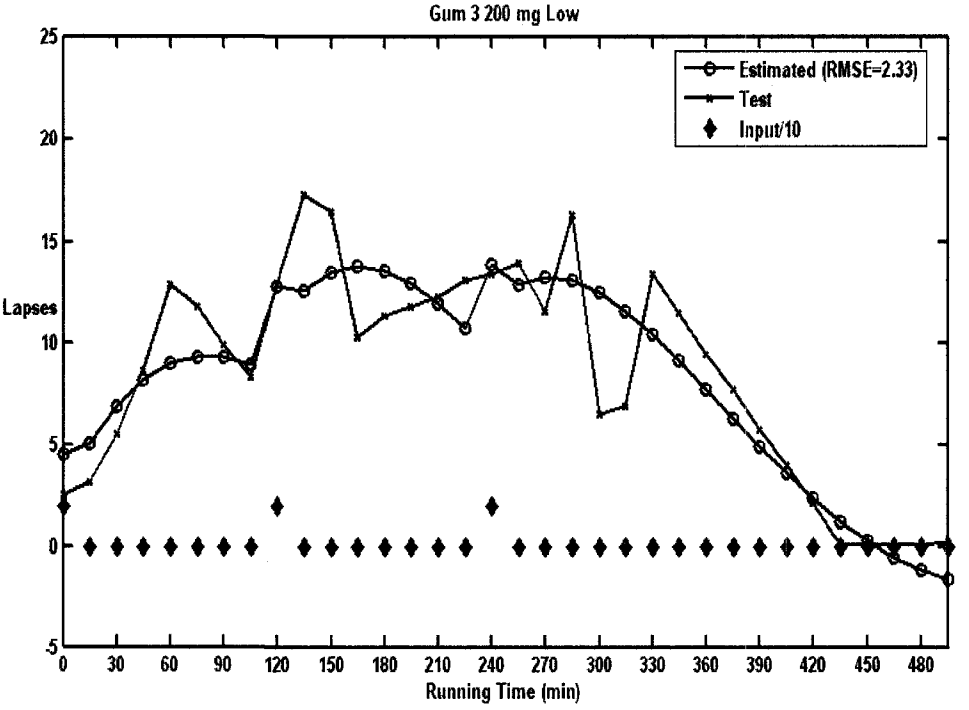

Figure 5.5: Caffeine model developed for the differential effects between the Gum 3 200 mg low-user and placebo cases using population averages.

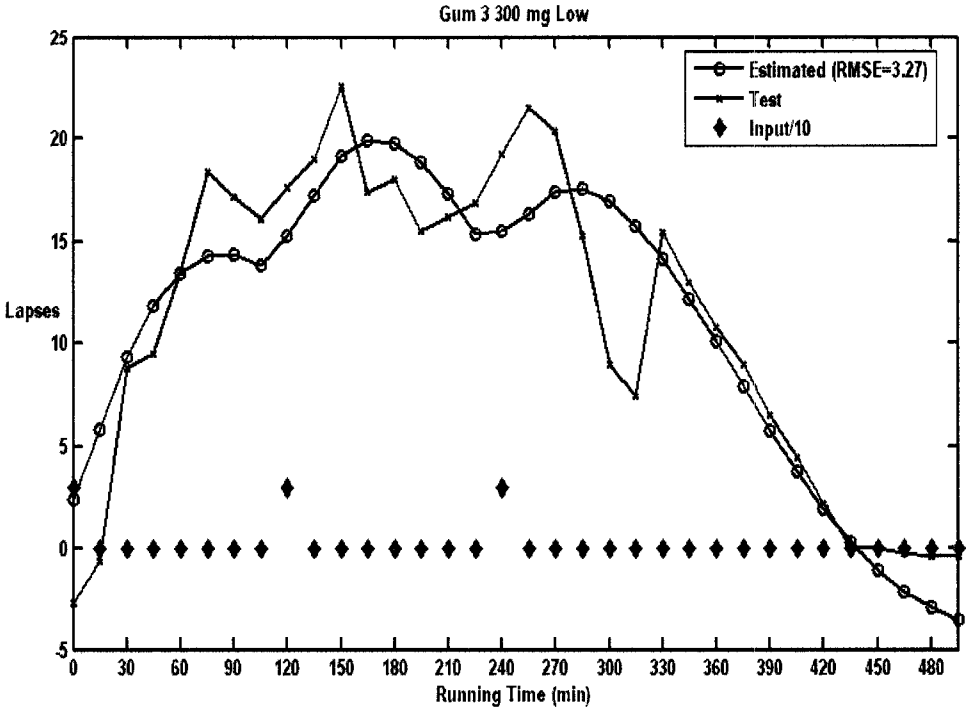

Figure 5.6: Caffeine model developed for the differential effects between the Gum 3 300 mg low-user and placebo cases using population averages.

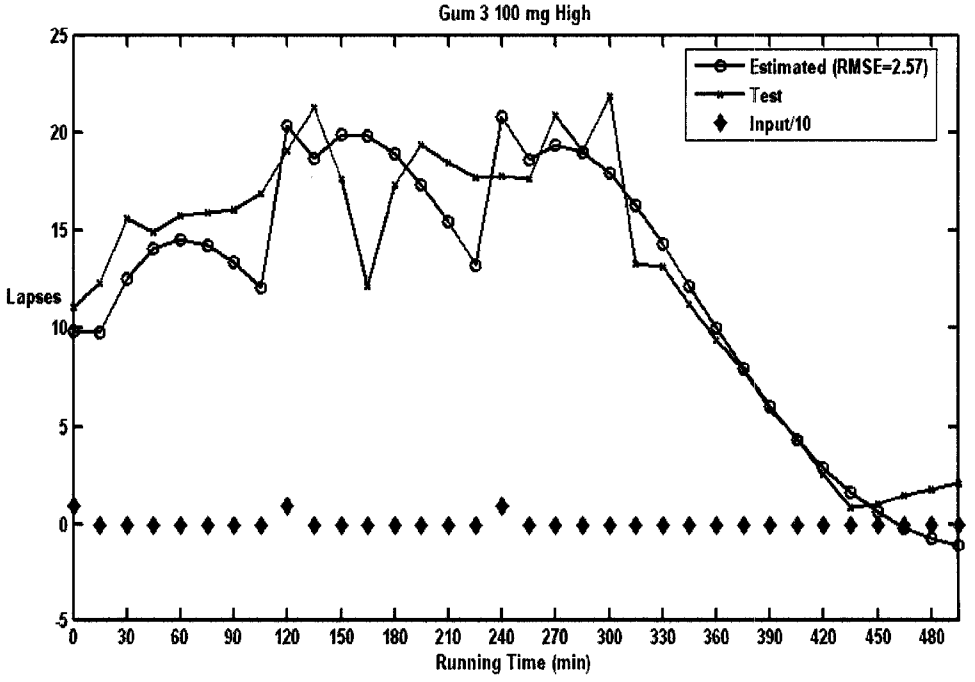

Figure 5.7 Caffeine model developed for the differential effects between the Gum 3 100 mg high-user and placebo cases using population averages.

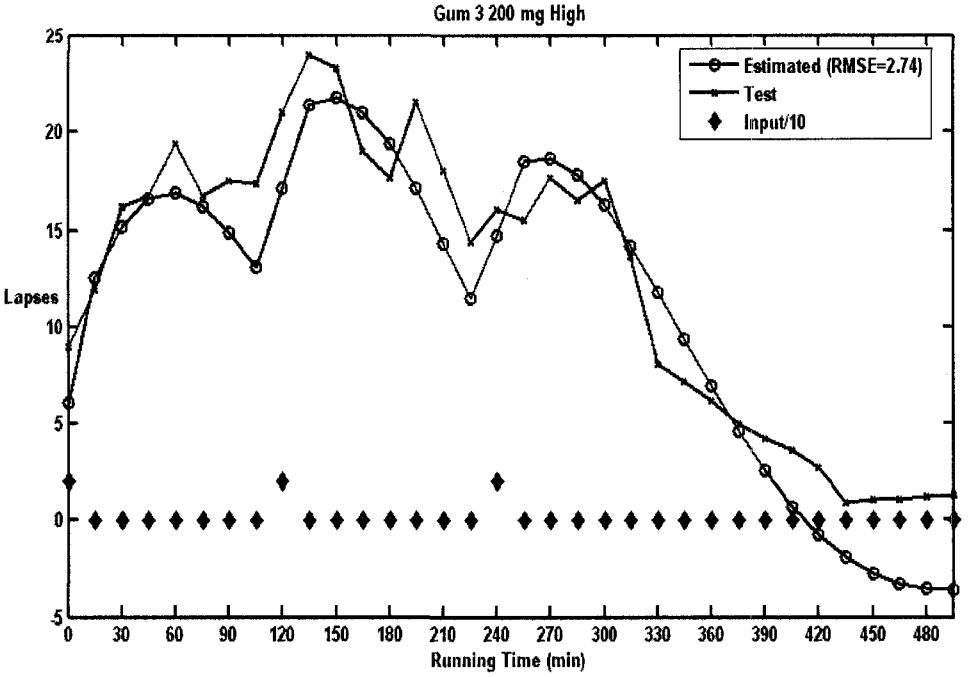

Figure 5.8: Caffeine model developed for the differential effects between the Gum 3 200 mg high-user and placebo cases using population averages.

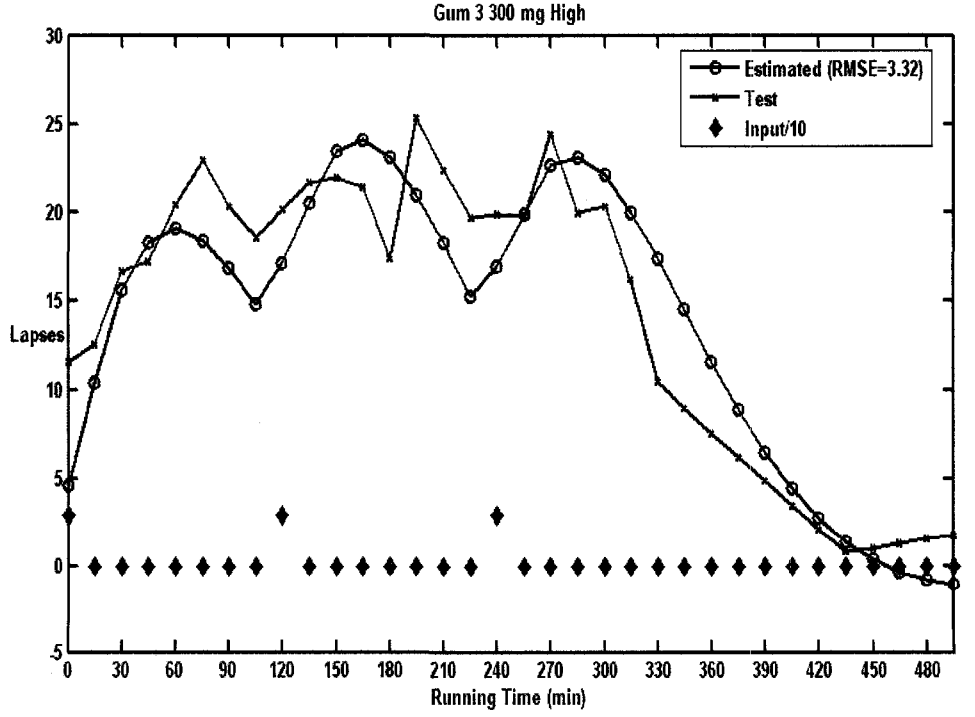

Figure 5.9: Caffeine model developed for the differential effects between the Gum 3 300 mg high-user and placebo cases using population averages.

5.2 Input Noise Effect

As shown in Figure 3.7, the caffeine input is structured as impulses proportional to the caffeine dose with additive white process noise. However, the additive noise is not completely white because of the limited input data points processed. A different noise pattern used for model identification would impact the modeling error. Figure 5.11 shows that root mean squared error (RMSE) of an identified model can be reduced when more input noise patterns are processed. In this study, for each input/output data set, the system identification process is repeated for 5,000 different input noise patterns. An optimal noise pattern is selected for each data set with a minimum modeling error from identified models. Figure 5.10 shows the noise pattern is selected as the best one for Gum 3 200 mg high-user from 5,000 different input patterns.

The effect of input noise level on modeling error is also studied. Three different noise levels (3%, 5% and 10%), the ratio of the variances of the signals, are investigated (see Table 5.1). The result shows that the effect of input noise level on the accuracy of the identified model is negligible. In this study, 5% input noise level is used for all caffeine model identification cases.

Table 5.1: Noise Level Effect on Estimation Errors (RMSE) (2nd order)

Data Set		Dose (mg)	Noise		
			3%	5%	10%
GUM 2 (AVG)		50	2.37	2.37	2.25
		100	1.83	1.83	1.76
		200	1.89	1.83	1.83
GUM 3 (AVG)	Low	100	2.57	2.57	2.57
		200	2.33	2.33	2.33
		300	3.32	3.27	3.38
	High	100	2.62	2.57	2.62
		200	3.91	2.74	2.80
		300	3.67	3.32	3.27

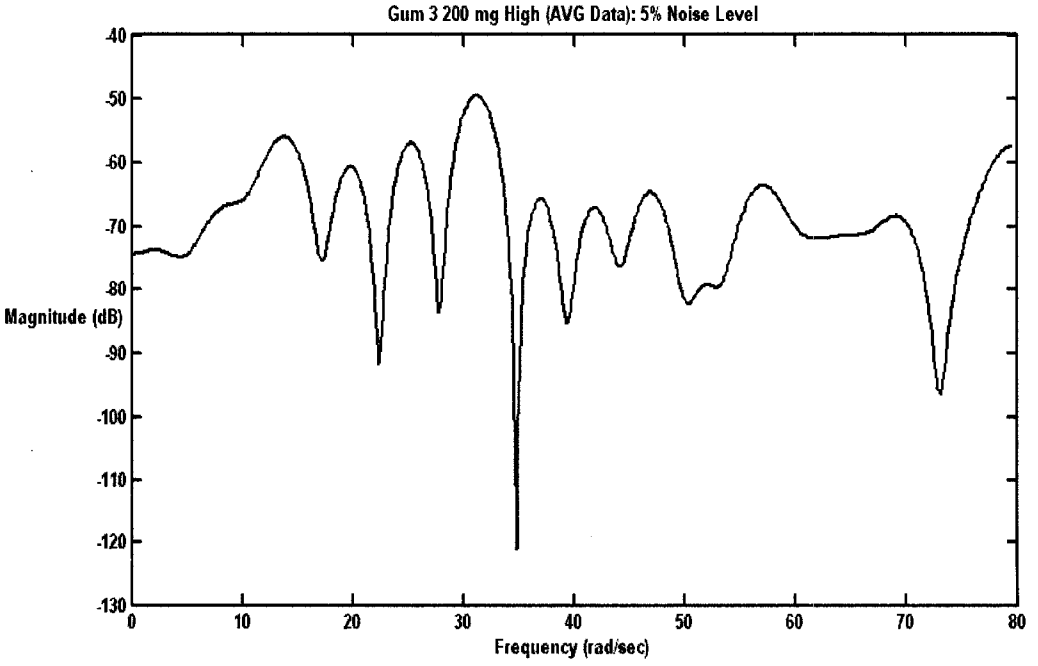

Figure 5.10: The best input noise pattern for Gum 3 200 mg high-user.

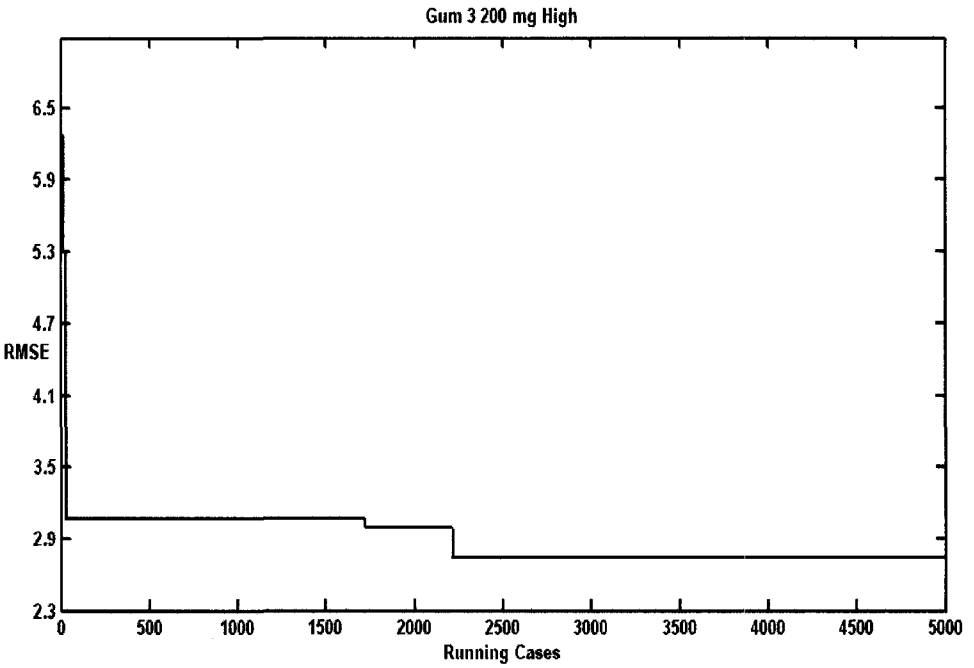

Figure 5.11: Modeling errors (RMSE) as a function of number of additive input noise patterns used for running Gum 3 200 mg high-user data.

5.3 Optimal Caffeine Model Order

In this section, effect of the model order on the accuracy of an identified model is studied. For each case, 5,000 input noise patterns with 5% noise level are used. Table 5.2 and Figure 5.12 show that as compared to a second-order model, here is no clear advantage to using a third-order model for both Gum 2 and Gum 3 population averages. Therefore in this study, a second-order caffeine model is used for all test data.

Table 5.2: Modeling Order Effect on Estimation Errors (RMSE) (5% noise)

Data Set		Dose (mg)	Model Order		
			1st	2nd	3rd
GUM 2 (AVG)		50	2.74	2.37	2.49
		100	2.49	1.83	1.52
		200	2.31	1.83	1.89
GUM 3 (AVG)	Low	100	4.14	2.57	2.04
		200	3.44	2.33	2.16
		300	5.42	3.27	3.15
	High	100	3.97	2.57	2.39
		200	4.72	2.74	3.03
		300	5.42	3.32	3.32

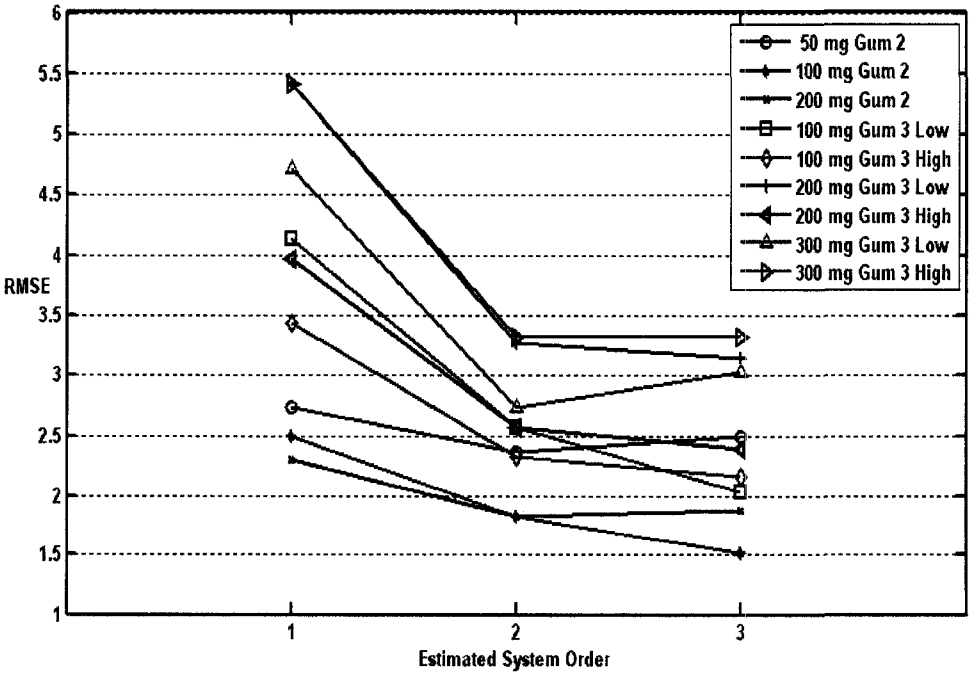

Figure 5.12: Modeling errors (RMSE) as a function of estimated system order.

5.4 State-space Model in Controllable Canonical Form

Since the identified state-space model is not unique, several potential model structures are considered. As shown in section 5.1, the second-order ARX model can be described as

$$y(k)+a_1y(k-1)+a_2y(k-2)=b_0u(k)+b_1u(k-1)+b_2u(k-2)$$

Its equivalent discrete transfer function model is

$$\frac{Y(z)}{U(z)}=\frac{b_0z^2+b_1z+b_2}{z^2+a_1z+a_2}$$

The corresponding state-space model in controllable canonical form is

$$x(k+1)=Ax(k)+Bu(k),\quad y(k)=Cx(k)+Du(k)$$

$$\mathrm{A}=\begin{bmatrix}0 & 1\\ -a_2 & -a_1\end{bmatrix},\ \mathrm{B}=\begin{bmatrix}0\\ 1\end{bmatrix},$$

$$\mathrm{C}=\begin{bmatrix}b_2-a_2b_0 & b_1-a_1b_0\end{bmatrix}=\begin{bmatrix}c_1 & c_2\end{bmatrix},\ \mathrm{D}=b_0=d_0 \tag{5.1}$$

This state-space model in controllable canonical form is proposed as the caffeine model due to its simplicity and convenience to be merged into a two-process model with circadian and homeostatic effects for future study. In this caffeine model structure, only five system parameters $[a_1,a_2,c_1,c_2,d_0]$ need to be identified. Table 5.3 shows all the

identified model coefficients from the population averages. It is noted that the first two coefficients $[a_1, a_2]$ (see Table 5.4) have small variations for both low and high users of caffeine among all doses. This indicates that the caffeine dosage (see Table 5.5 and Figure 5.13) and habitual usage (see Table 5.6 and Figure 5.14) do not have much impact on caffeine model dynamics controlled by system matrices A and B.

Table 5.3: Identified Model Coefficients from Population Averages

Data Set		Dose (mg)	a_1	a_2	c_1	c_2	d_0	RMSE
GUM 2 (AVG)		50	-1.571	0.609	0.212	0.391	-0.162	2.37
		100	-1.715	0.766	0.170	0.077	0.062	1.83
		200	-1.562	0.600	0.041	0.146	0.034	1.83
GUM 3 (AVG)	Low	100	-1.750	0.794	-0.044	0.487	0.446	2.57
		200	-1.793	0.827	-0.106	0.252	0.226	2.33
		300	-1.792	0.833	-0.037	0.193	0.083	3.27
	High	100	-1.702	0.748	-0.410	0.978	0.981	2.57
		200	-1.753	0.803	-0.342	0.629	0.306	2.74
		300	-1.632	0.693	-0.046	0.348	0.156	3.32

Table 5.4: Model Coefficients from Population Averages

Parameters	GUM 2		GUM 3	
	Mean	STD	Mean	STD
a_1	-1.616	0.086	-1.737	0.061
a_2	0.658	0.094	0.783	0.054
c_1	0.141	0.089	-0.164	0.167
c_2	0.205	0.165	0.481	0.290
d_0	-0.022	0.122	0.366	0.326

Table 5.5: Dose Effect from Population Averages

Parameters		50mg	100mg	200mg	300mg
a_1	Mean	-1.571	-1.722	-1.703	-1.712
	STD	-	0.025	0.123	0.113
a_2	Mean	0.609	0.769	0.743	0.763
	STD	-	0.023	0.125	0.099

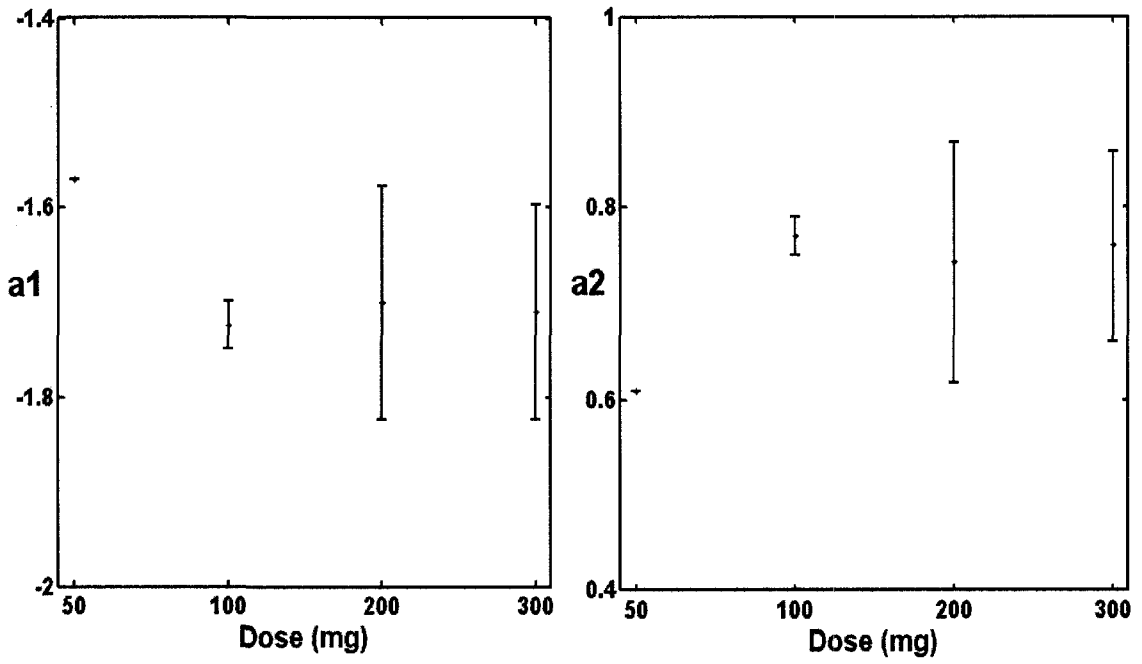

Figure 5.13: Dose effect from population averages

Table 5.6: Habitual Effect from Population Averages

Parameters		Gum 3 High	Gum 3 Low
a_1	Mean	-1.696	-1.778
	STD.	0.061	0.025
a_2	Mean	0.748	0.818
	STD.	0.055	0.021

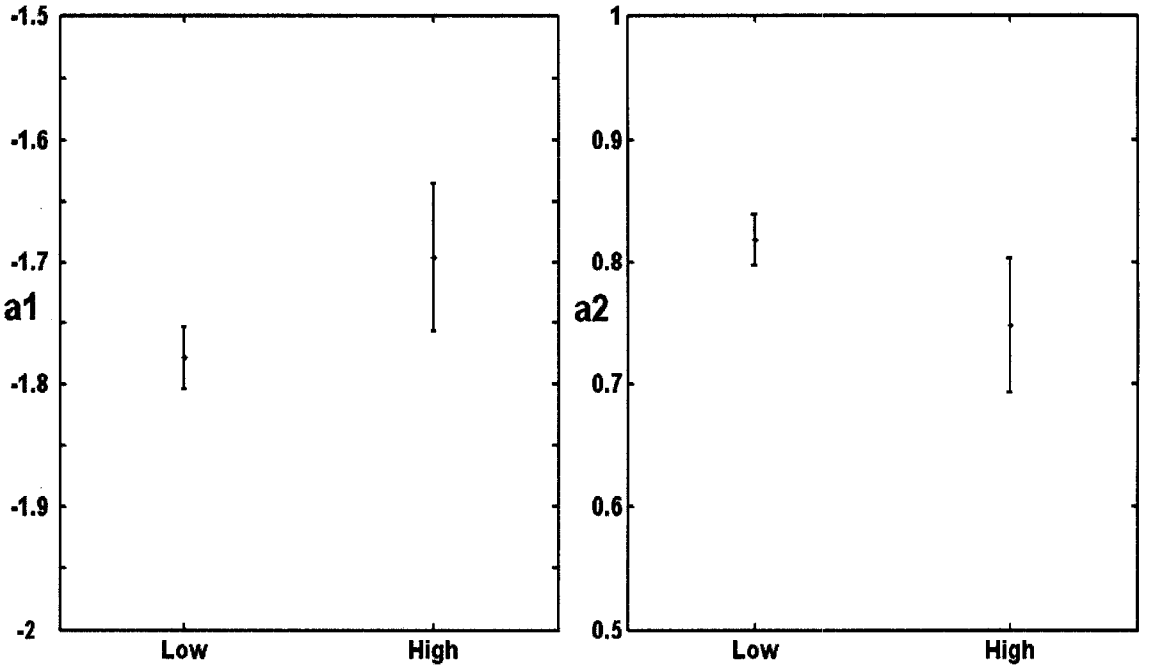

Figure 5.14: Habitual effect from population averages

5.5 Comparison of OKID and ARX Method

We also use the ARX model (autoregressive with exogenous input model) to identify the caffeine model for the Gum 2 and Gum 3 population average data.

The second-order ARX model can be described as

$$y(k)+a_1y(k-1)+a_2y(k-2)=b_0u(k)+b_1u(k-1)+b_2u(k-2)$$

Table 5.7 shows that as compared to a second-order OKID model, there is a clear disadvantage of using a second-order ARX model for both Gum 2 and Gum 3 population averages.

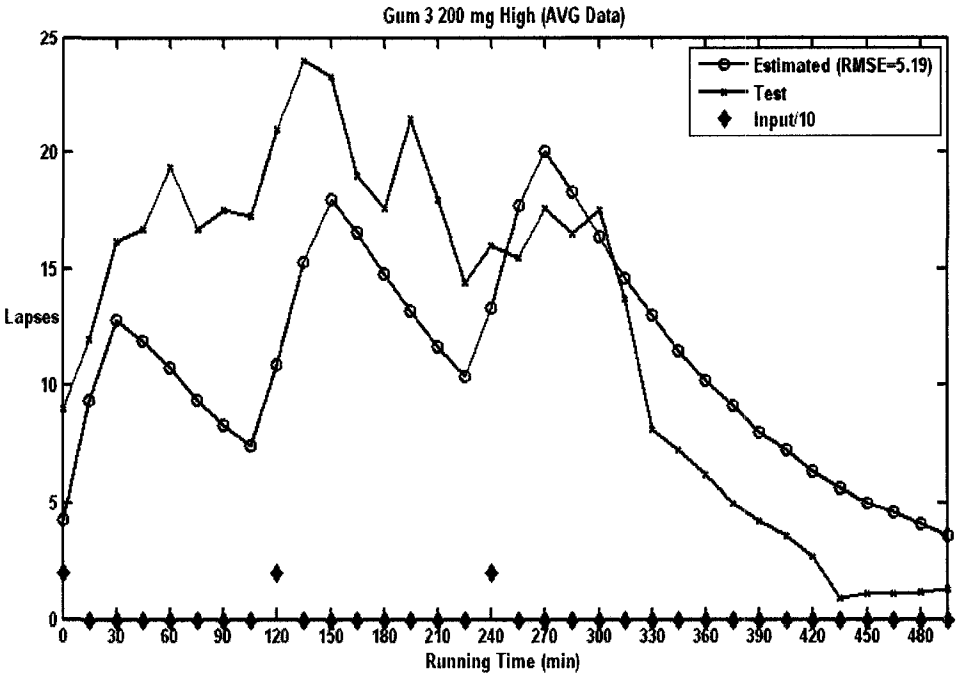

Figure 5.15: Estimation result using an ARX model (2nd order Least-Squares Model for Gum 3 200 mg high-users from population averages).

Table 5.7: Comparison of OKID and ARX Method

Data Set		Dose (mg)	Modeling Error	
			OKID	ARX
GUM 2 (AVG)		50	2.37	2.62
		100	1.83	2.43
		200	1.83	2.19
GUM 3 (AVG)	Low	100	2.57	3.91
		200	2.33	3.38
		300	3.27	4.90
	High	100	2.57	6.36
		200	2.74	5.19
		300	3.32	7.00

CHAPTER 6

IDENTIFICATION OF INDIVIDUALIZED CAFFEINE MODEL

The OKID algorithm is also used to identify the caffeine model for Gum 2 and Gum 3 individual subject data. For Gum 3 data, since the same subject was used repeatedly for placebo and other caffeine doses, caffeine-only data can be obtained by subtracting each individual subject performance data (100, 200 and 300 mg) from the placebo data (0 mg) for the same subject. However, for Gum 2 data, different subjects were used for different caffeine doses. So we use the placebo population average as the placebo data for each subject to calculate the caffeine-only data for all Gum 2 subjects.

6.1 Individualized Caffeine Model

Figures 6.1 to 6.69 show some of the individualized caffeine models developed for Gum 2 and Gum 3 subjects. The individualized caffeine model developed usually has a larger modeling error as compared to the caffeine model developed from the population average data shown in the previous section.

Table 6.1 to 6.4 and Figure 6.70 show identified model coefficients of individualized caffeine models from Gum 2 and Gum 3 data. It is also noted that the first two coefficients $[a_1, a_2]$ have small variations for both low and high users of caffeine among all doses. The result shows that the caffeine dosage (see Table 6.5 and Figure 6.71) and habitual usage (see Table 6.6 and Figure 6.72) do not have much impact on caffeine model dynamics.

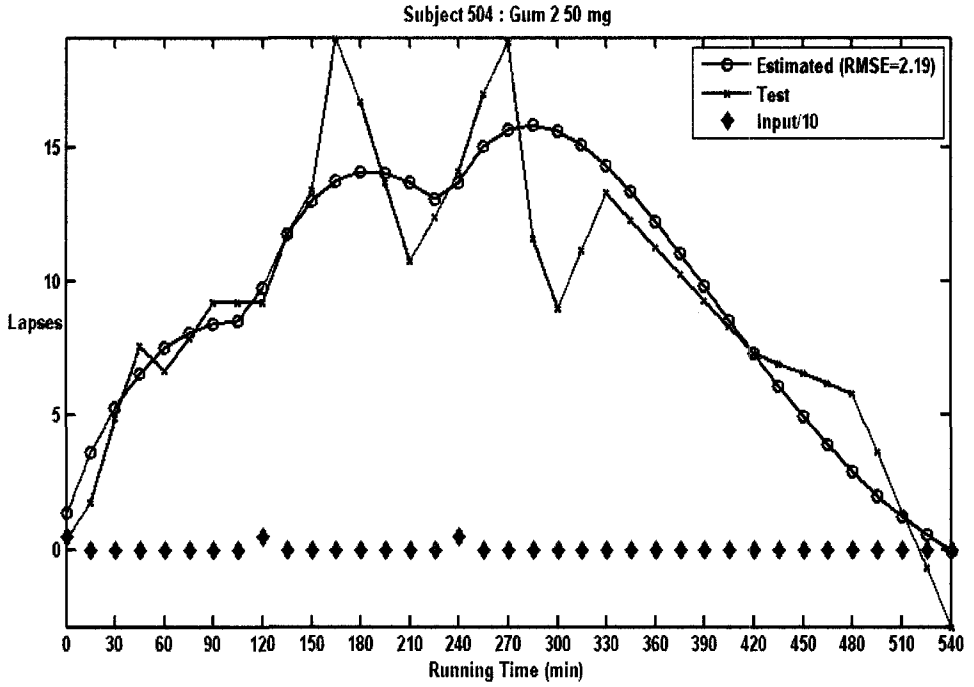

Figure 6.1: Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 504 data and population averages placebo data.

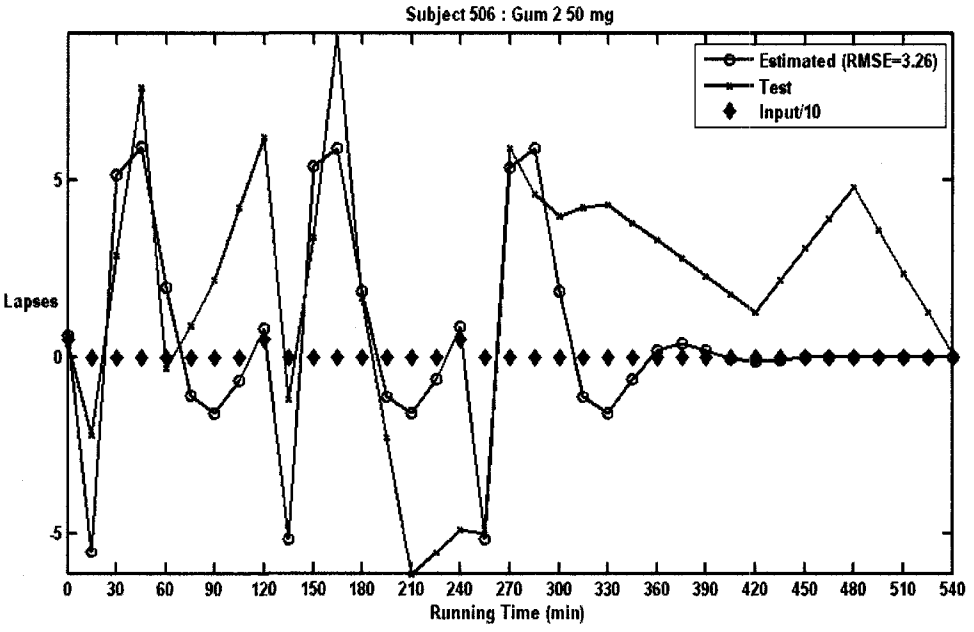

Figure 6.2: Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 506 data and population averages placebo data.

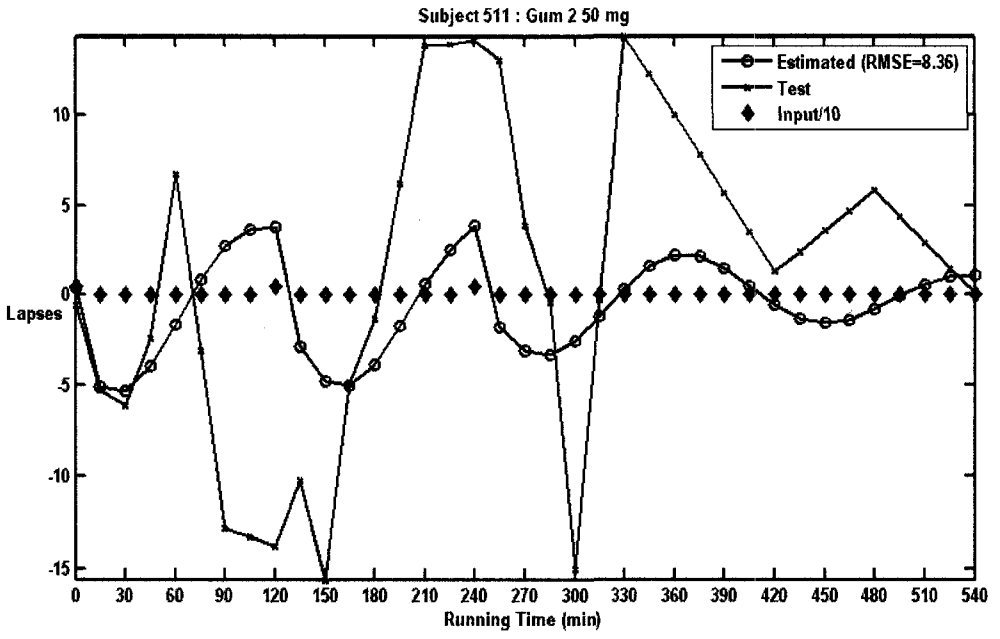

Figure 6.3: Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 511 data and population averages placebo data.

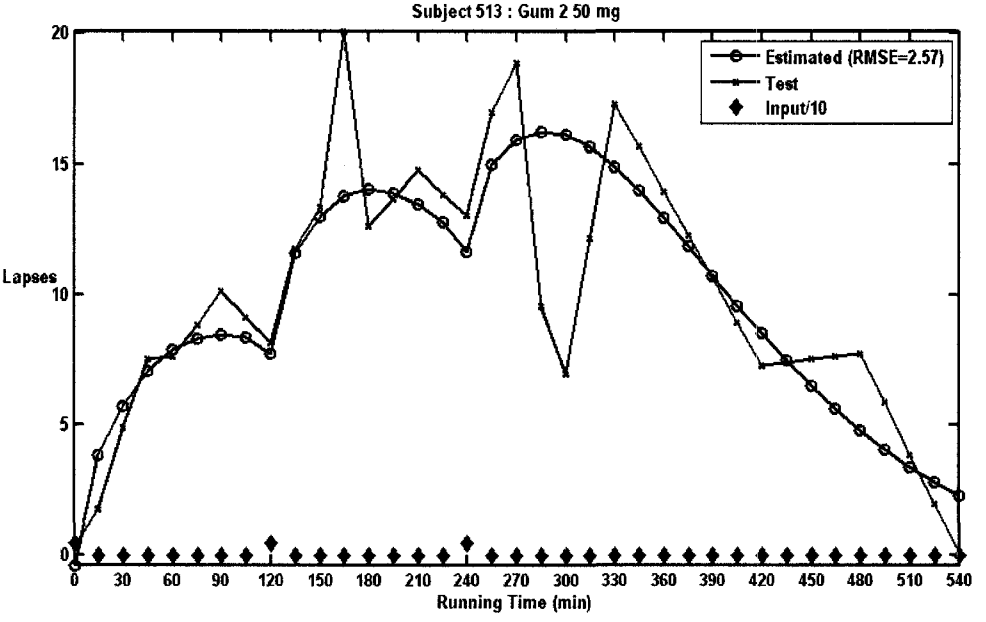

Figure 6.4: Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 513 data and population averages placebo data.

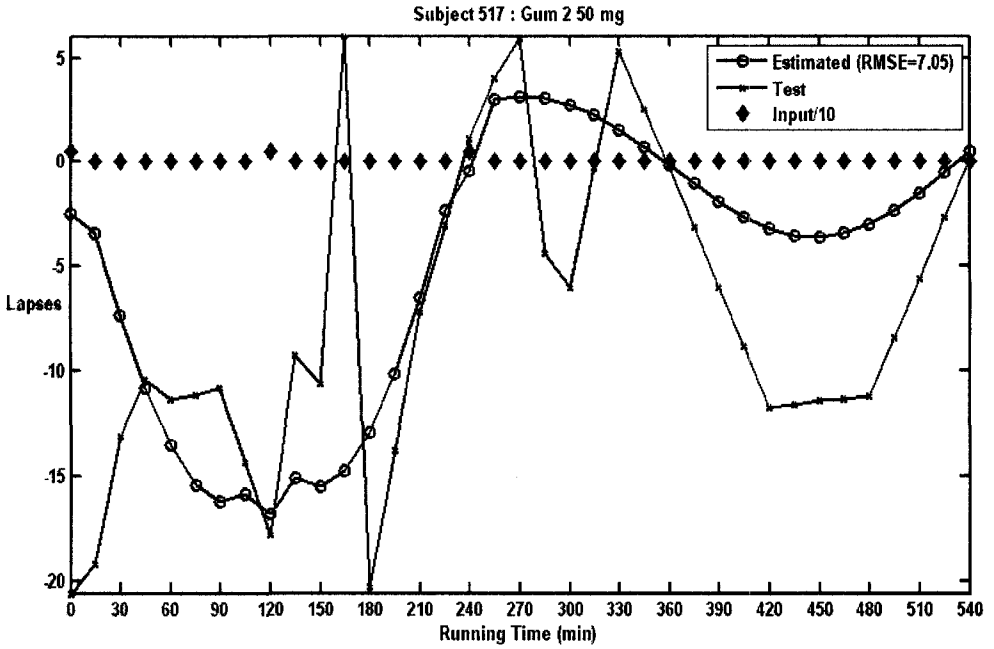

Figure 6.5: Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 517 data and population averages placebo data.

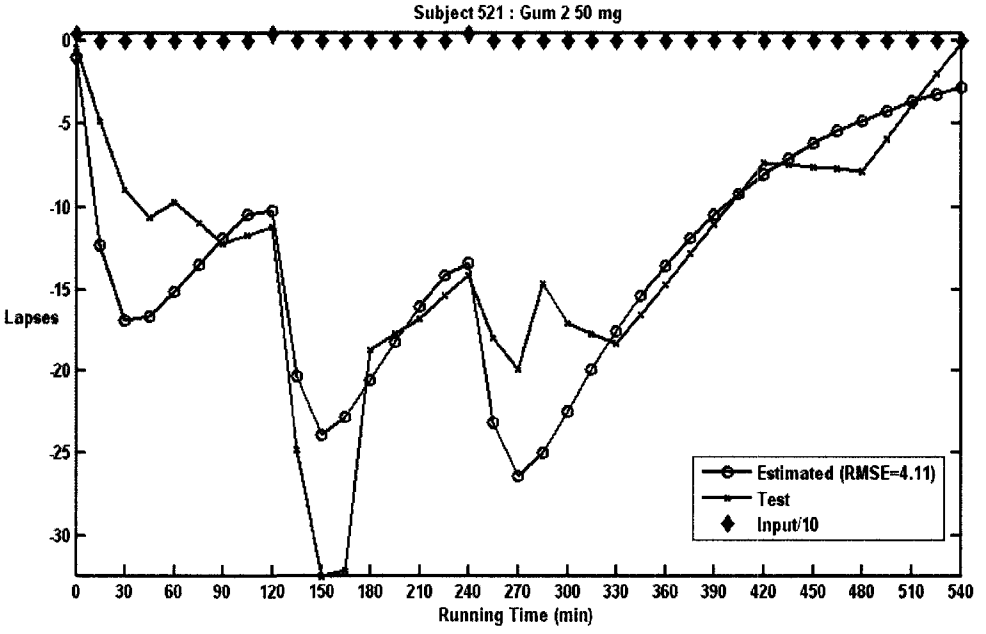

Figure 6.6: Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 521 data and population averages placebo data.

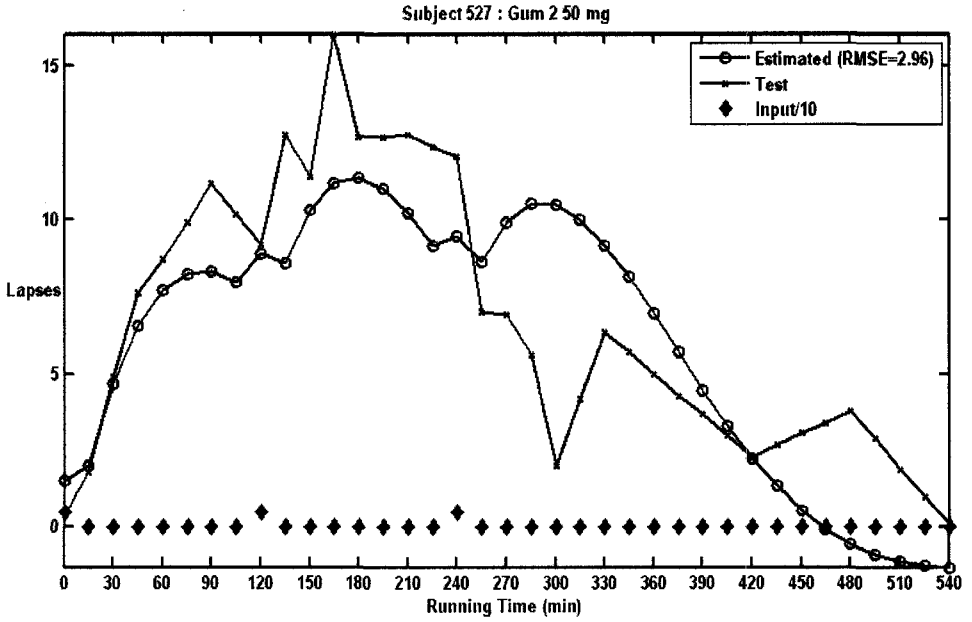

Figure 6.7: Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 527 data and population averages placebo data.

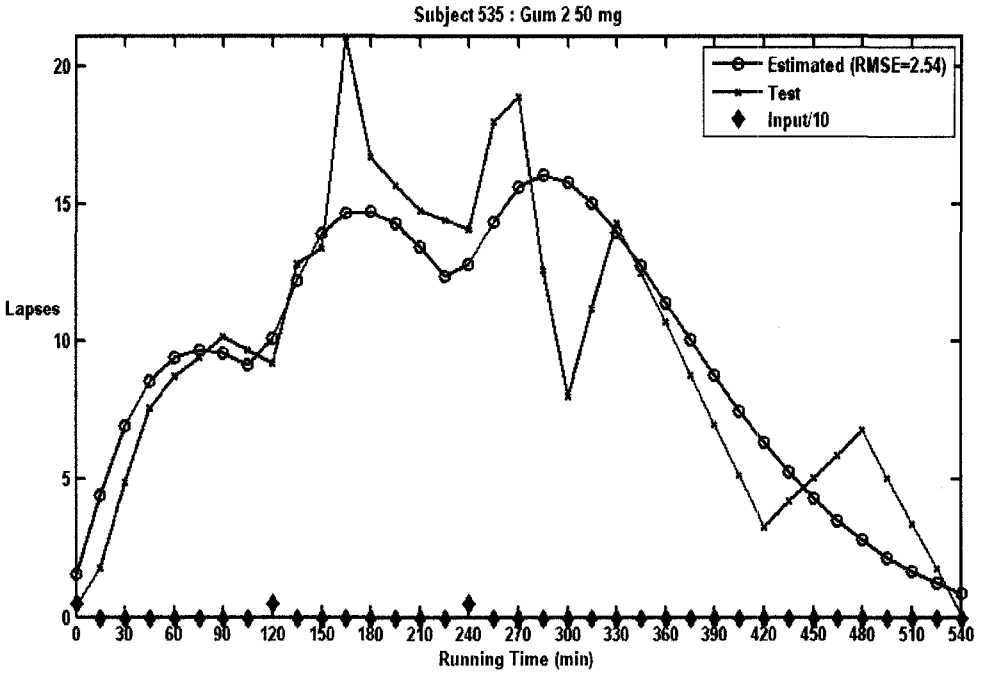

Figure 6.8: Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 535 data and population averages placebo data.

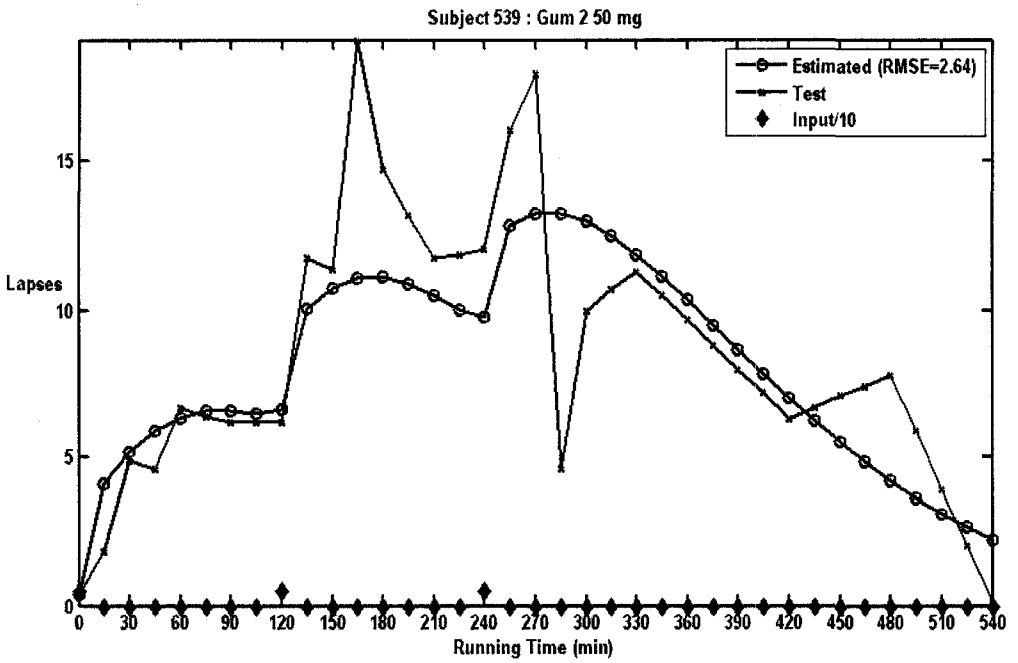

Figure 6.9: Individualized caffeine model developed for the differential effects between Gum 2 50 mg subject 539 data and population averages placebo data.

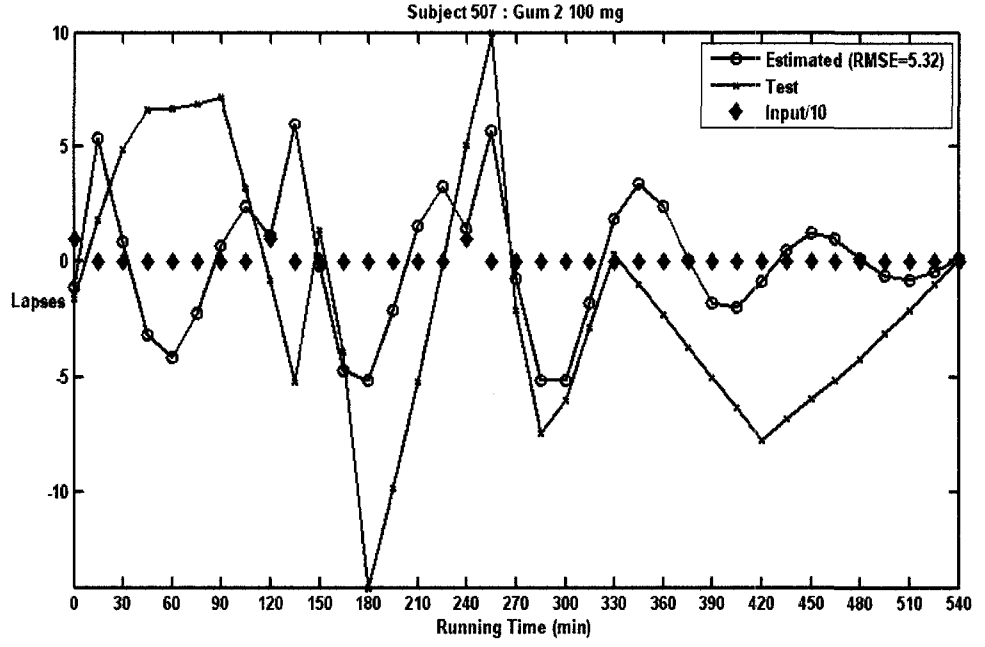

Figure 6.10: Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 507 data and population averages placebo data.

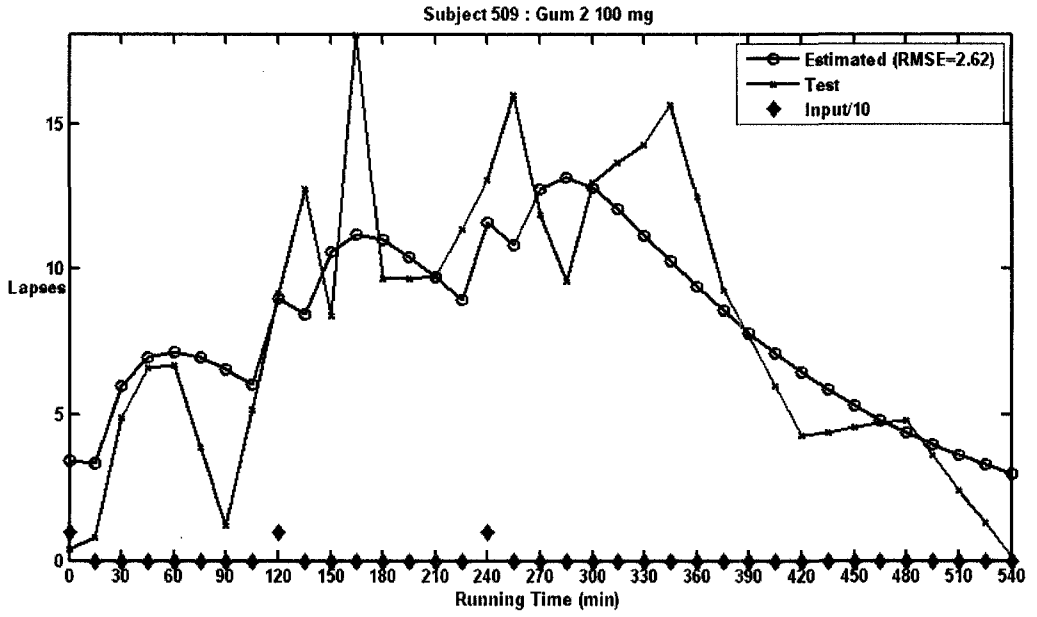

Figure 6.11: Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 509 data and population averages placebo data.

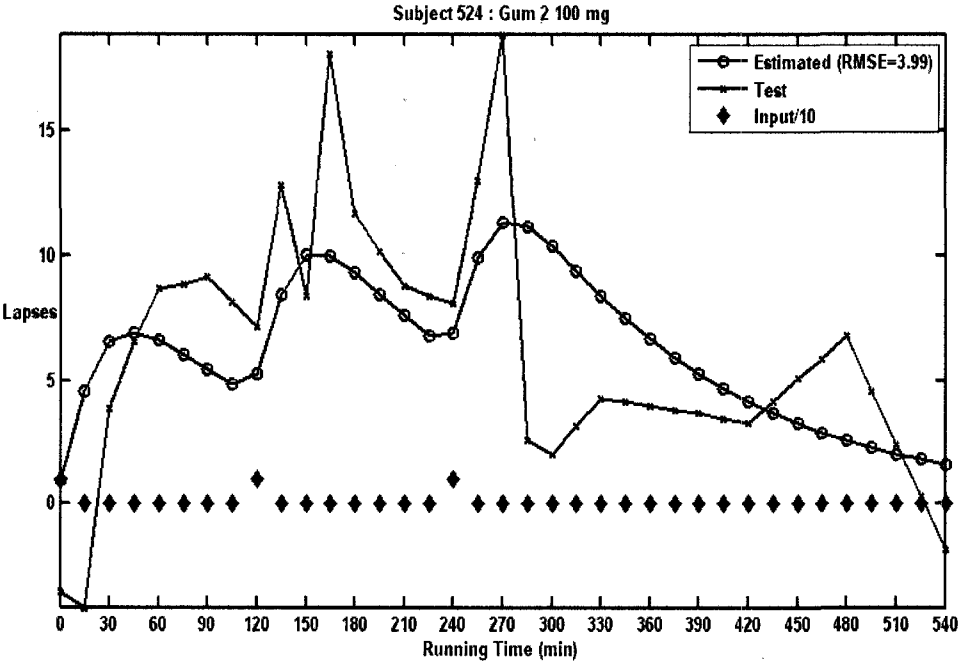

Figure 6.12: Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 524 data and population averages placebo data.

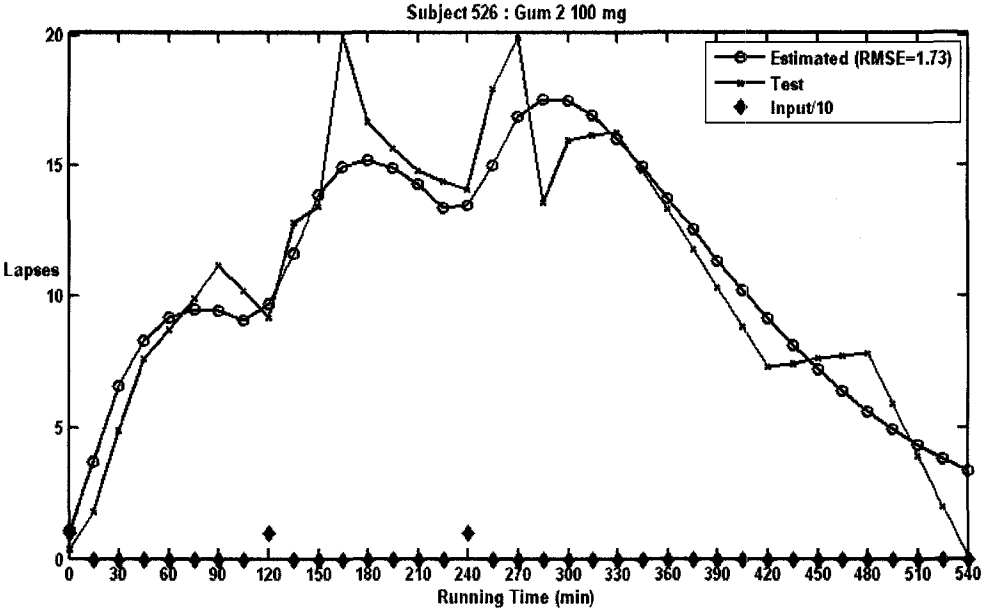

Figure 6.13: Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 526 data and population averages placebo data.

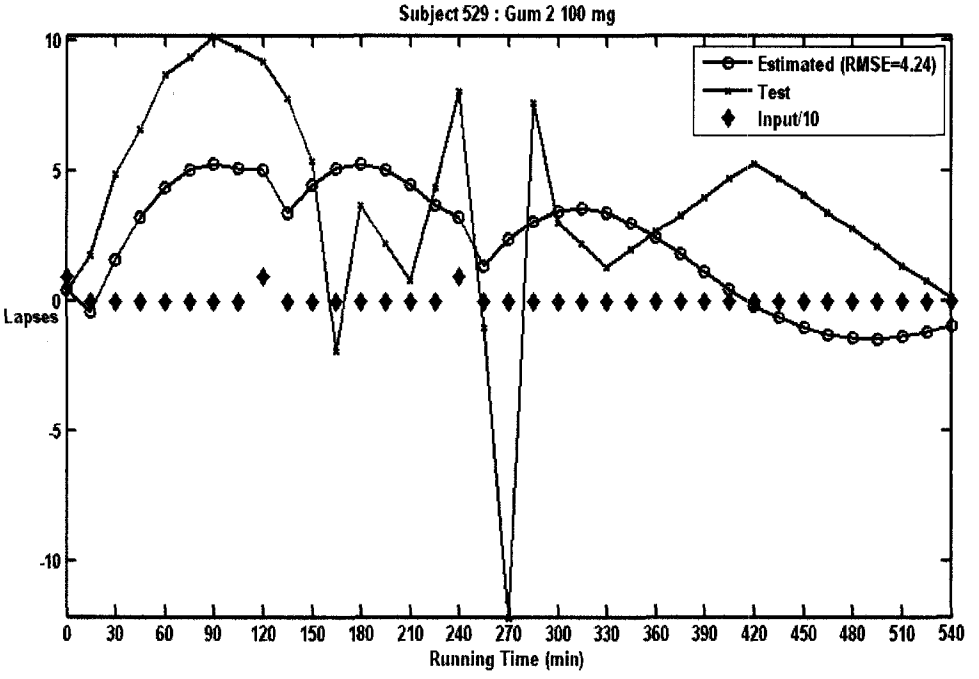

Figure 6.14: Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 529 data and population averages placebo data.

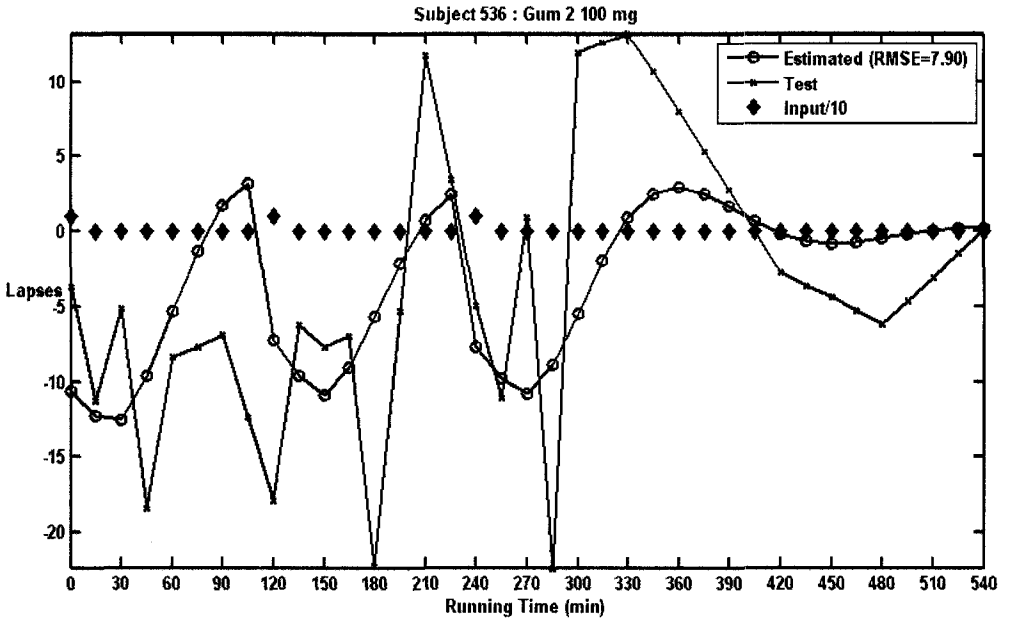

Figure 6.15: Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 536 data and population averages placebo data.

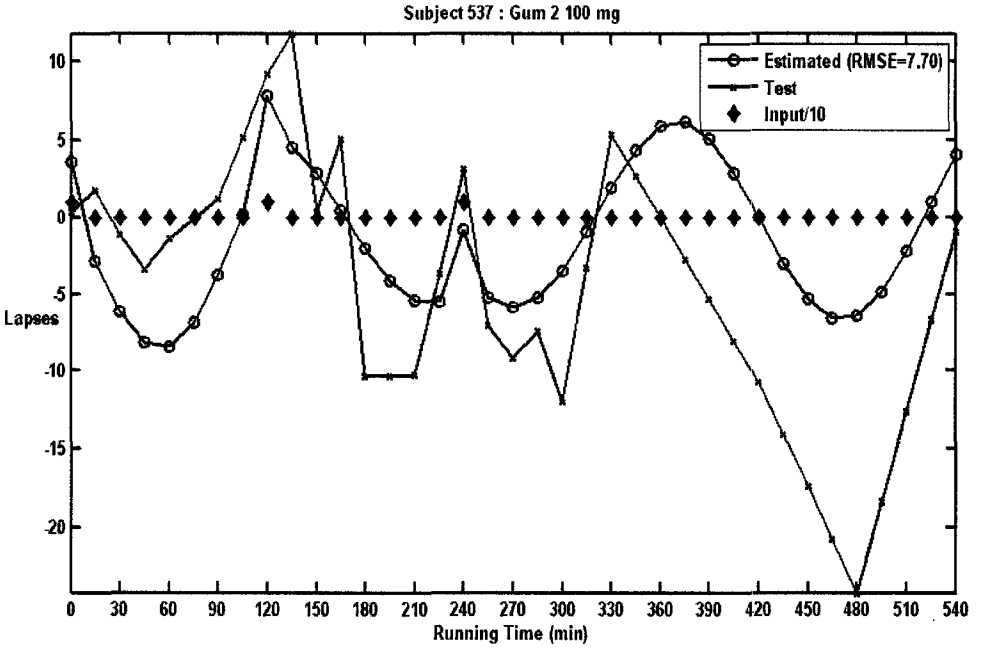

Figure 6.16: Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 537 data and population averages placebo data.

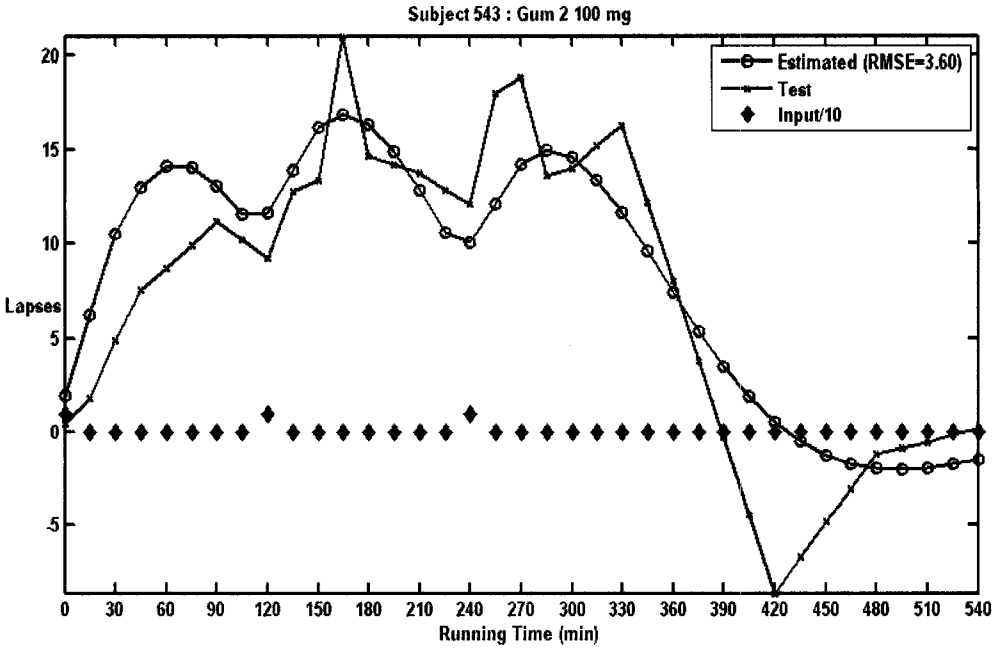

Figure 6.17: Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 543 data and population averages placebo data.

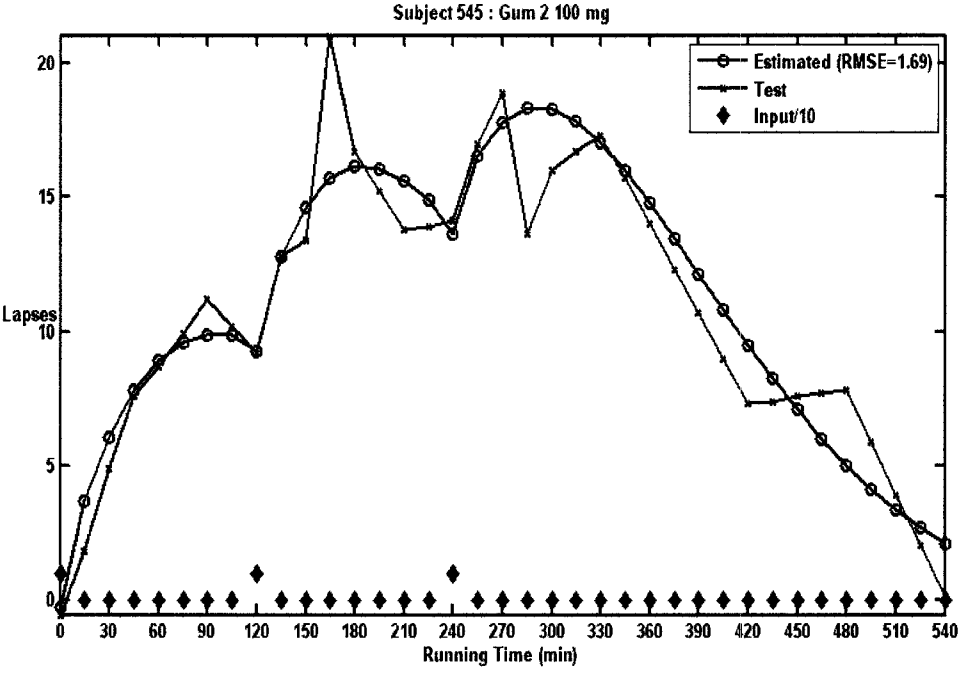

Figure 6.18: Individualized caffeine model developed for the differential effects between Gum 2 100 mg subject 545 data and population averages placebo data.

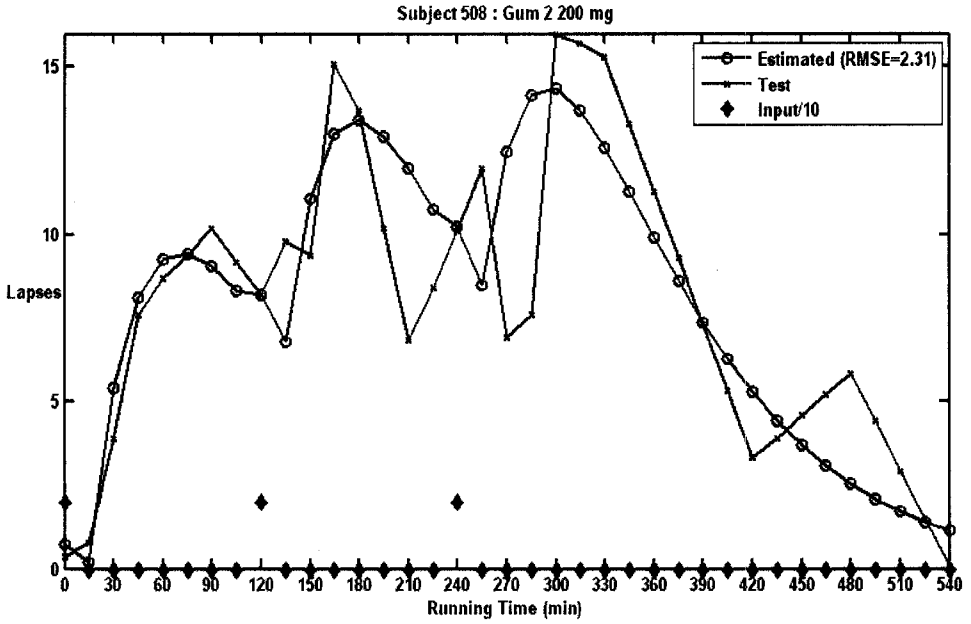

Figure 6.19: Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 508 data and population averages placebo data.

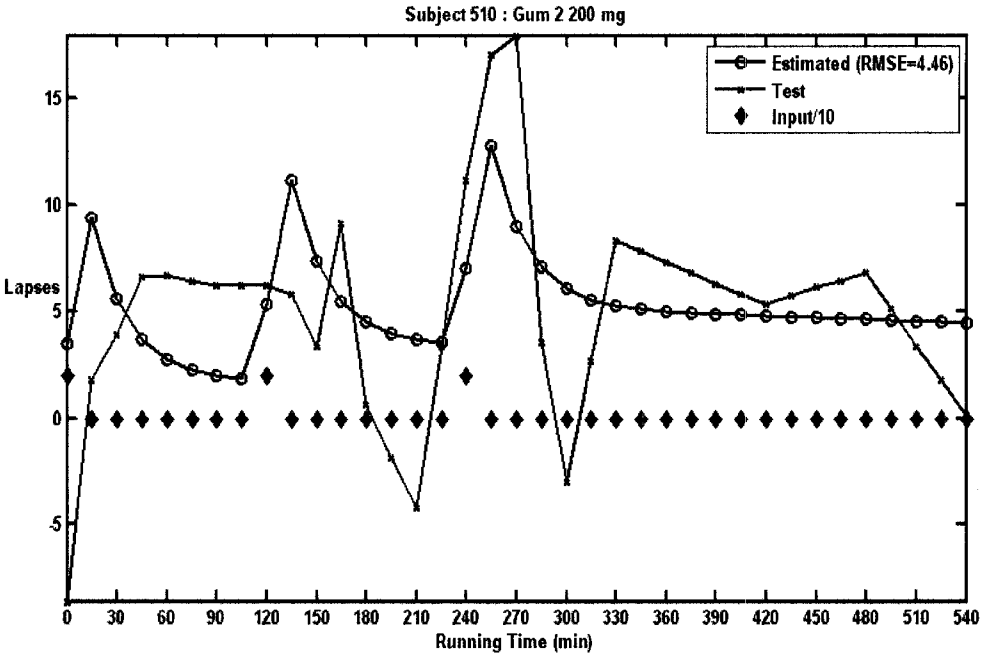

Figure 6.20: Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 510 data and population averages placebo data.

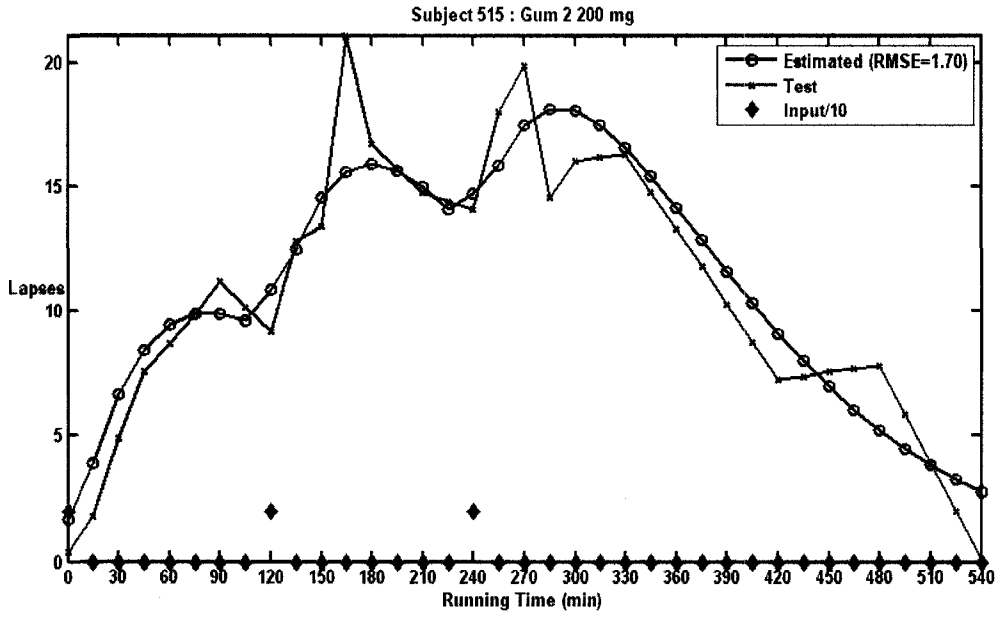

Figure 6.21: Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 515 data and population averages placebo data.

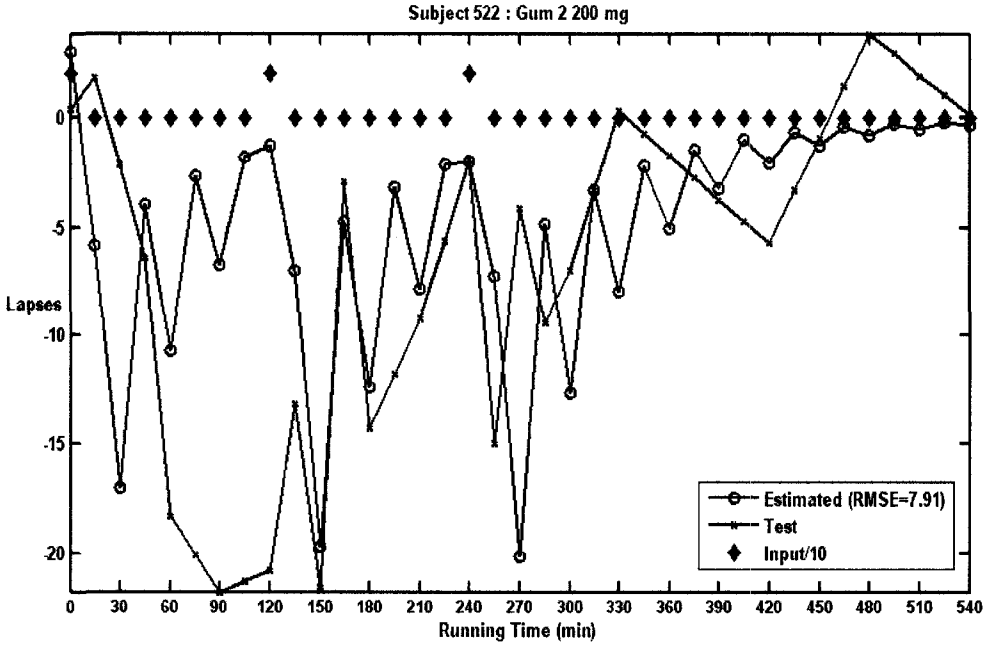

Figure 6.22: Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 522 data and population averages placebo data.

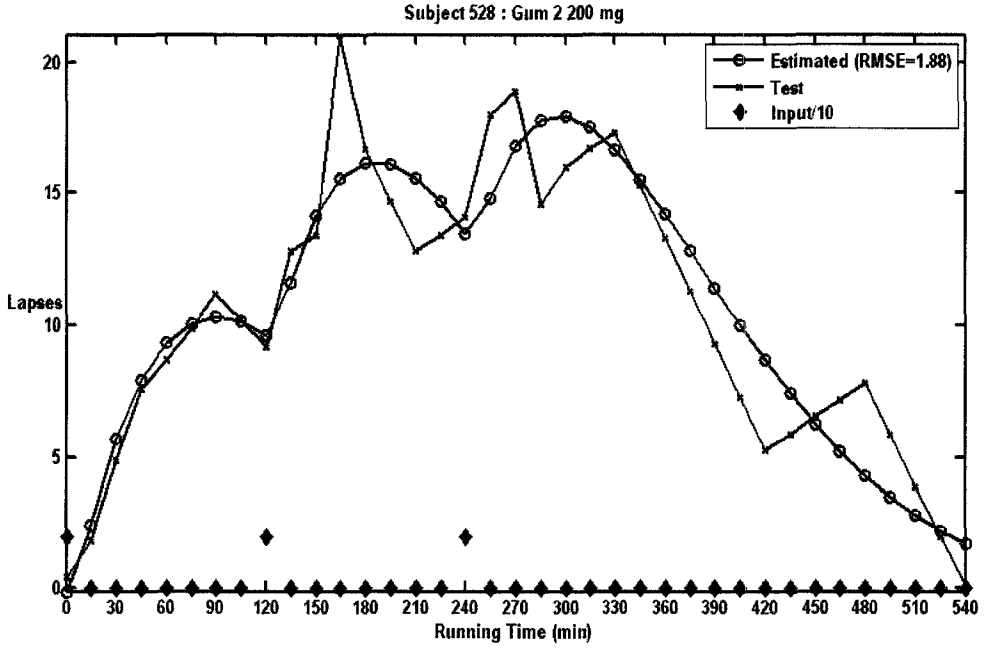

Figure 6.23: Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 528 data and population averages placebo data.

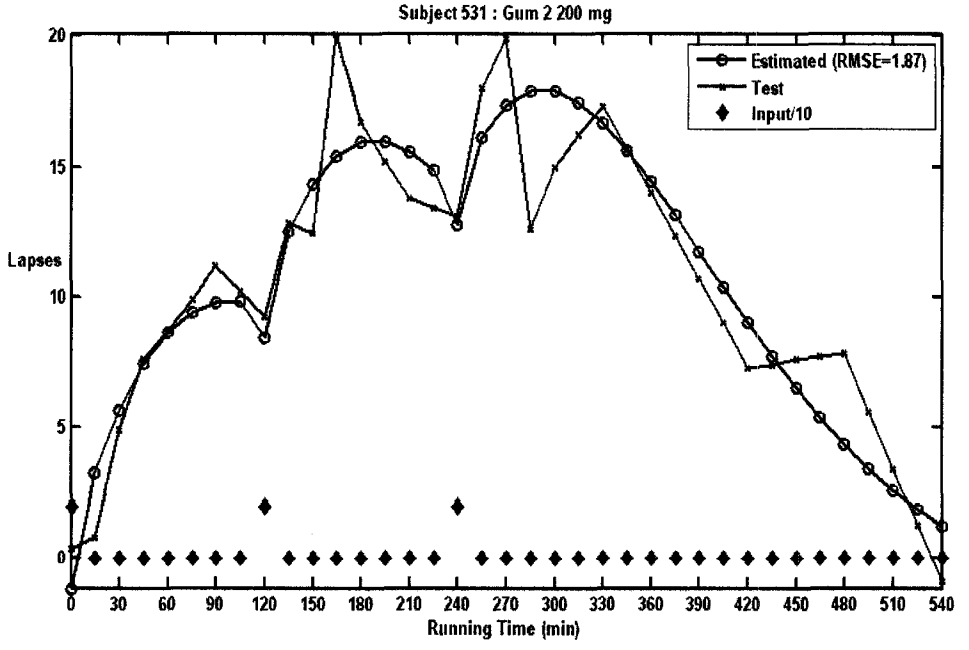

Figure 6.24: Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 531 data and population averages placebo data.

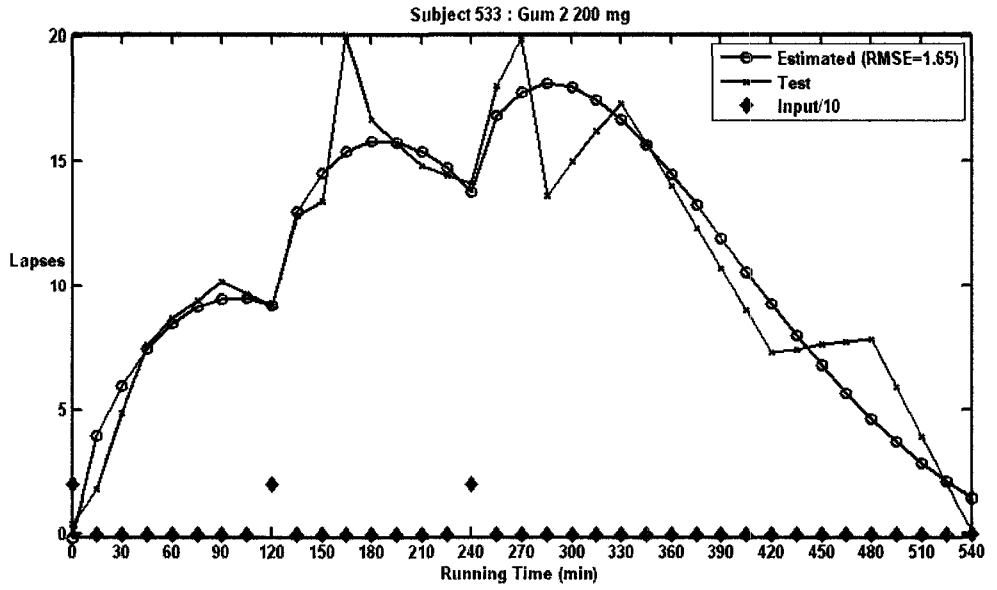

Figure 6.25: Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 533 data and population averages placebo data.

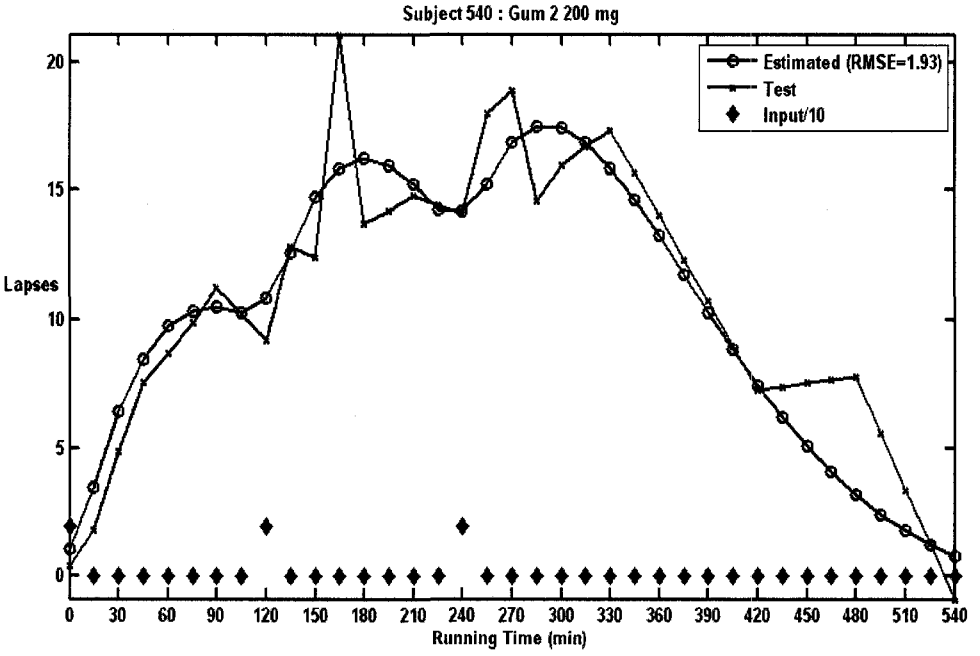

Figure 6.26: Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 540 data and population averages placebo data.

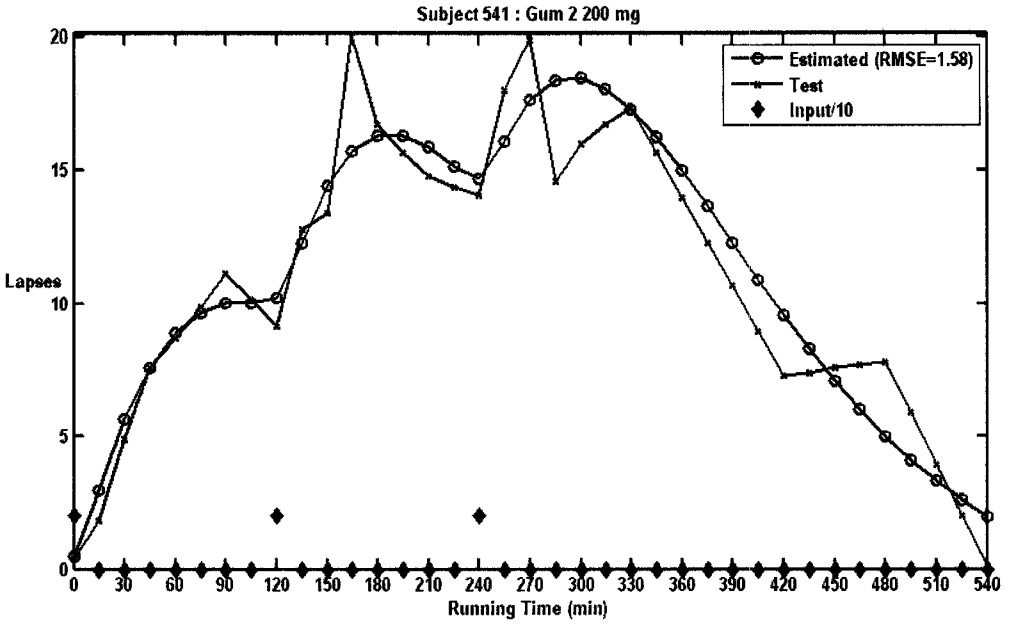

Figure 6.27: Individualized caffeine model developed for the differential effects between Gum 2 200 mg subject 541 data and population averages placebo data.

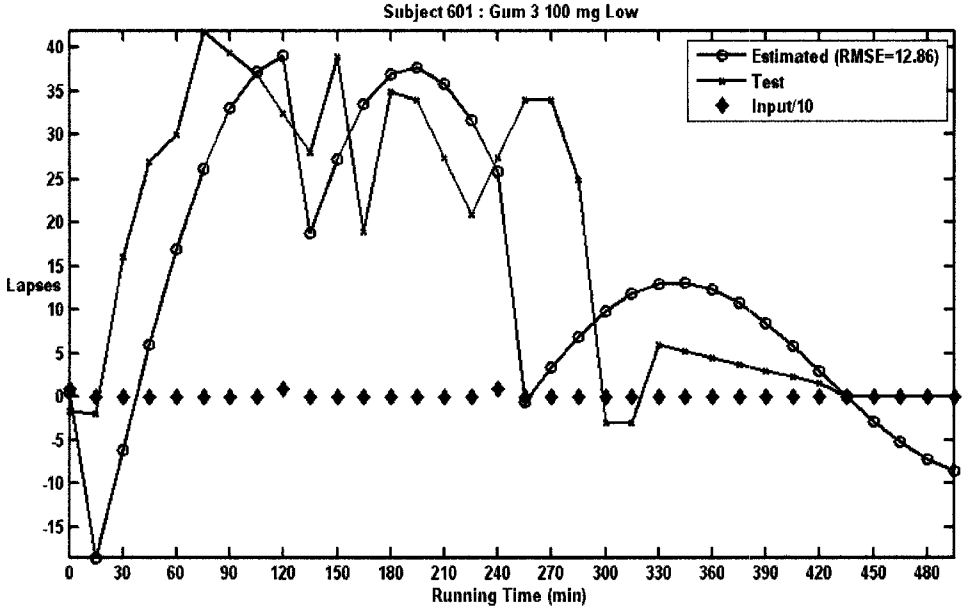

Figure 6.28: Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 601.

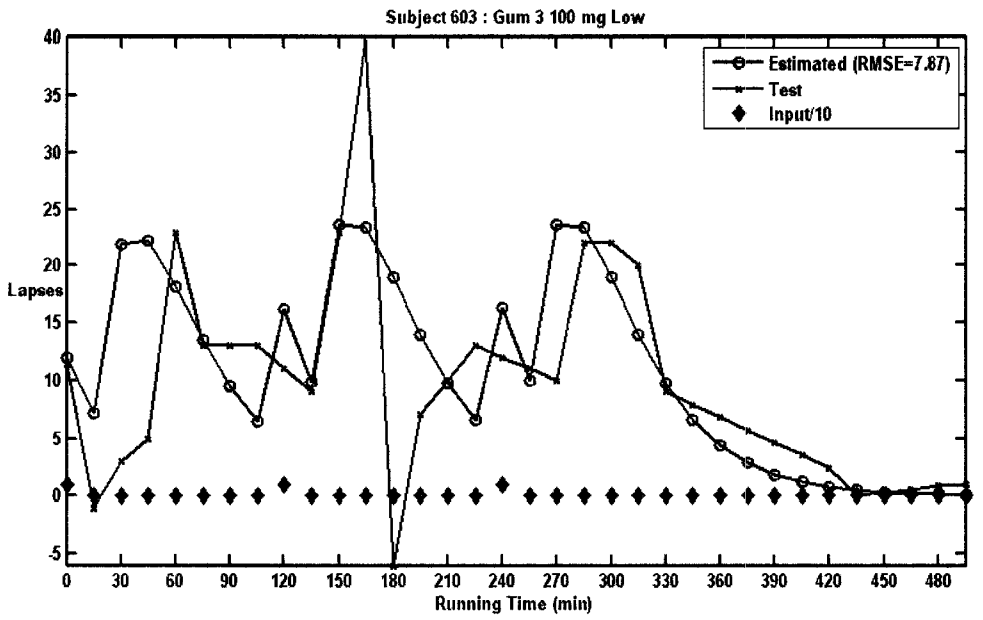

Figure 6.29: Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 603.

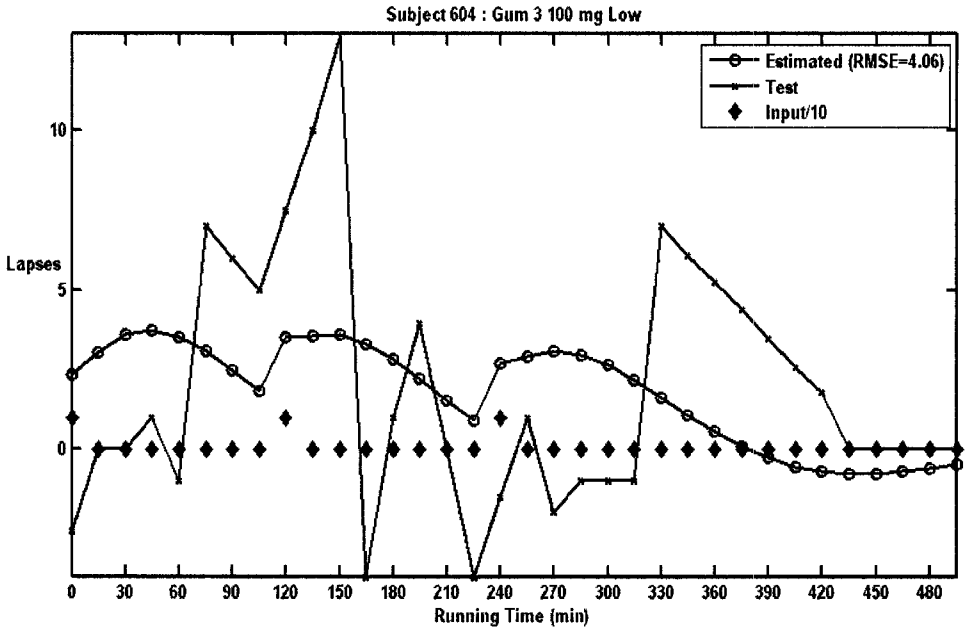

Figure 6.30: Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 604.

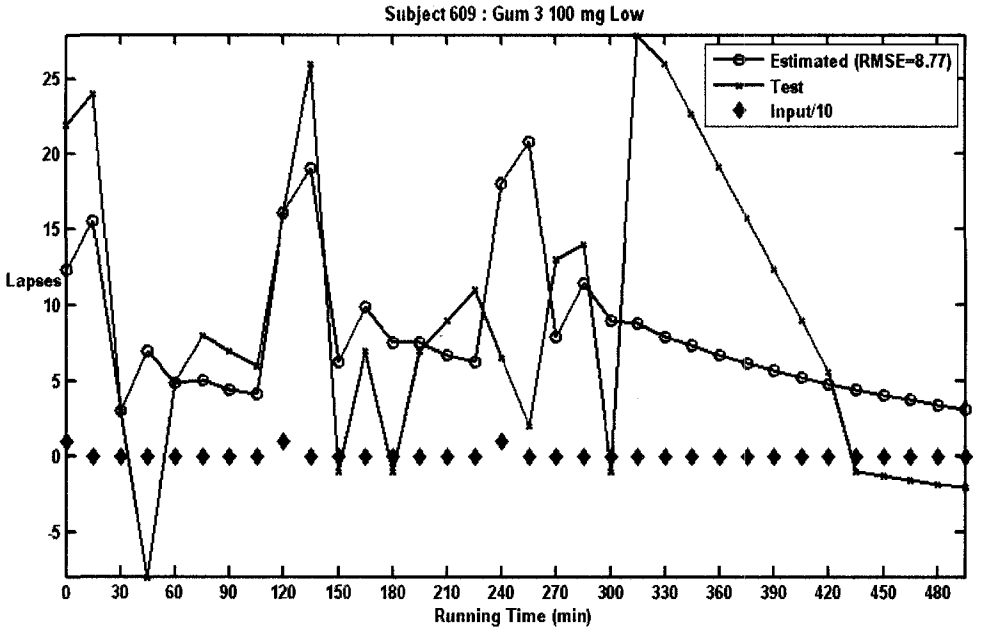

Figure 6.31: Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 609.

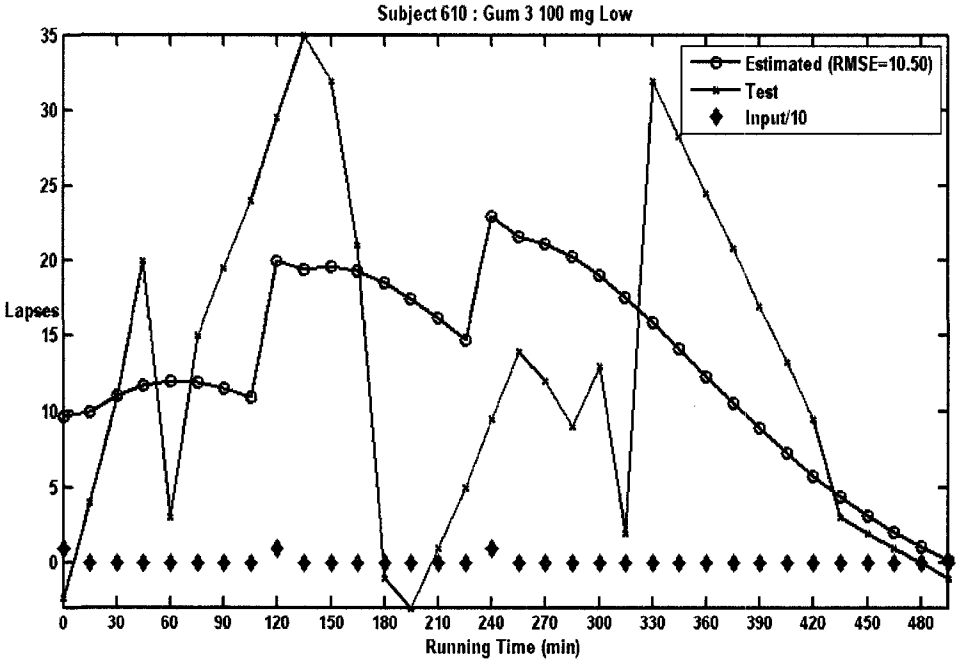

Figure 6.32: Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 610.

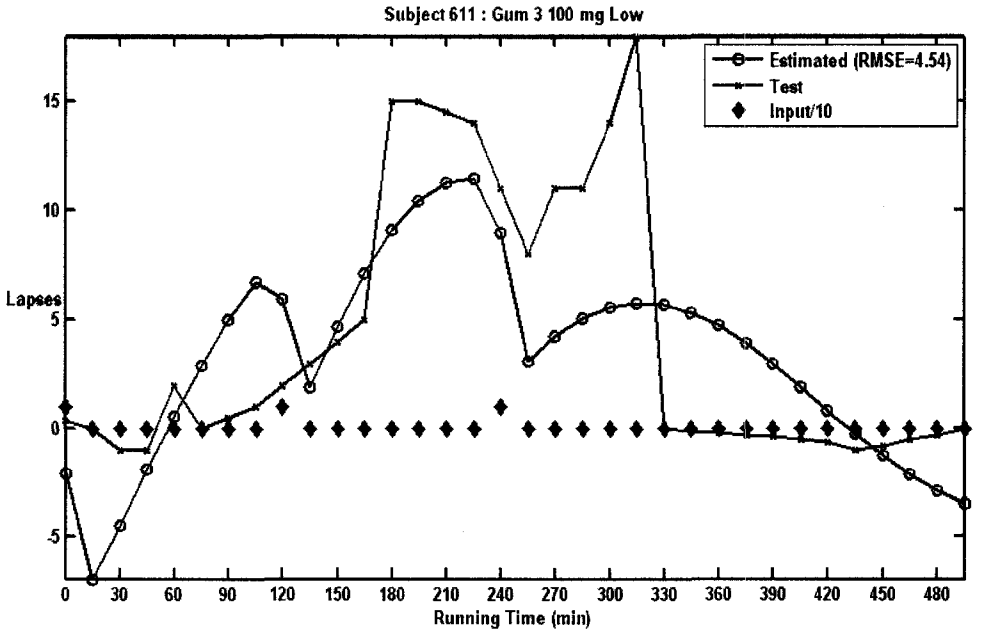

Figure 6.33: Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 611.

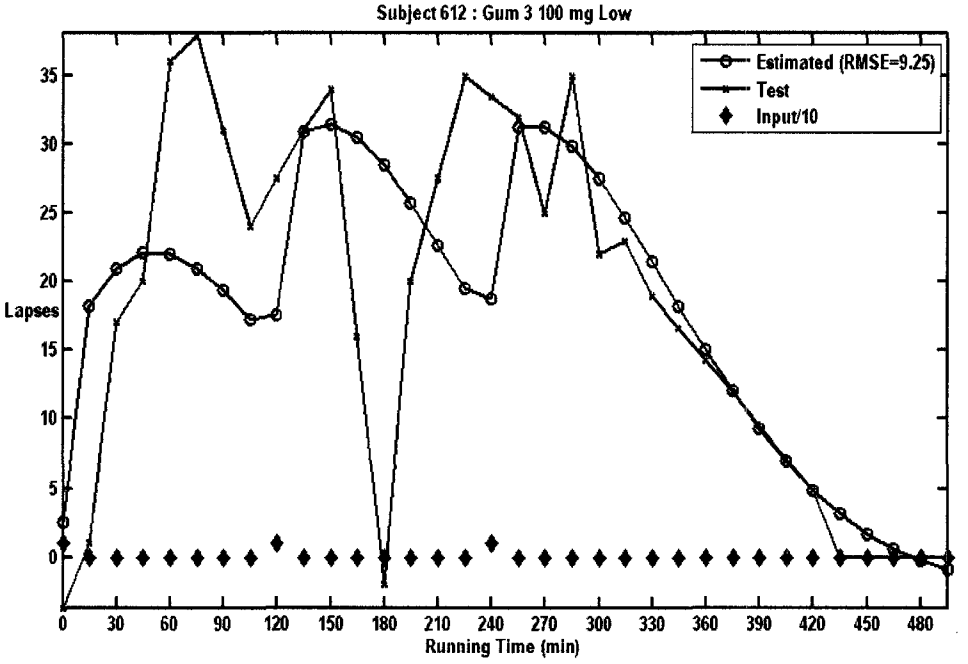

Figure 6.34: Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 612.

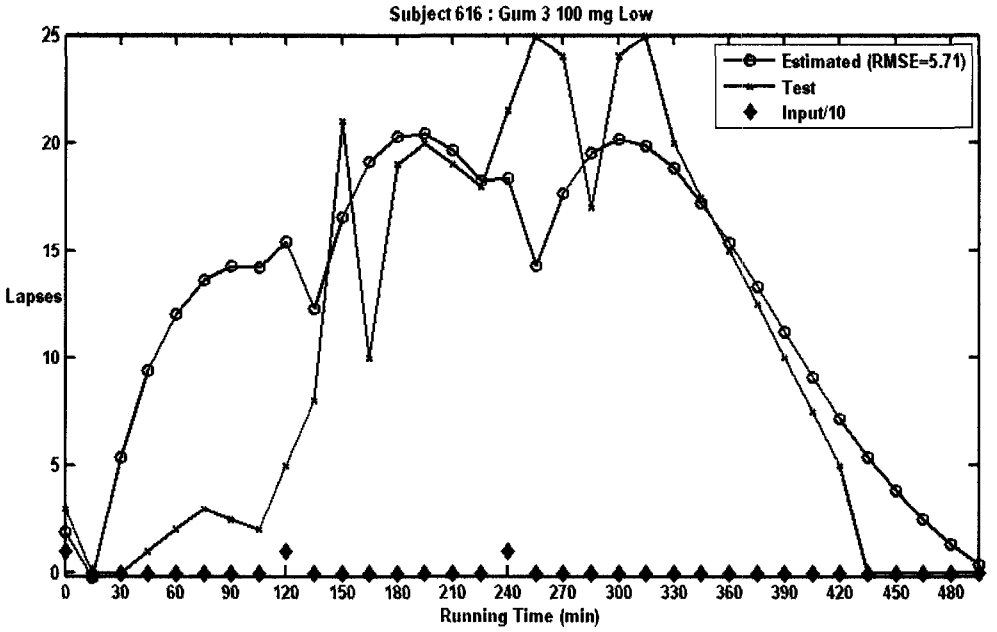

Figure 6.35: Individualized caffeine model developed for the differential effects between Gum 3 100 mg low-user data and placebo data for subject 616.

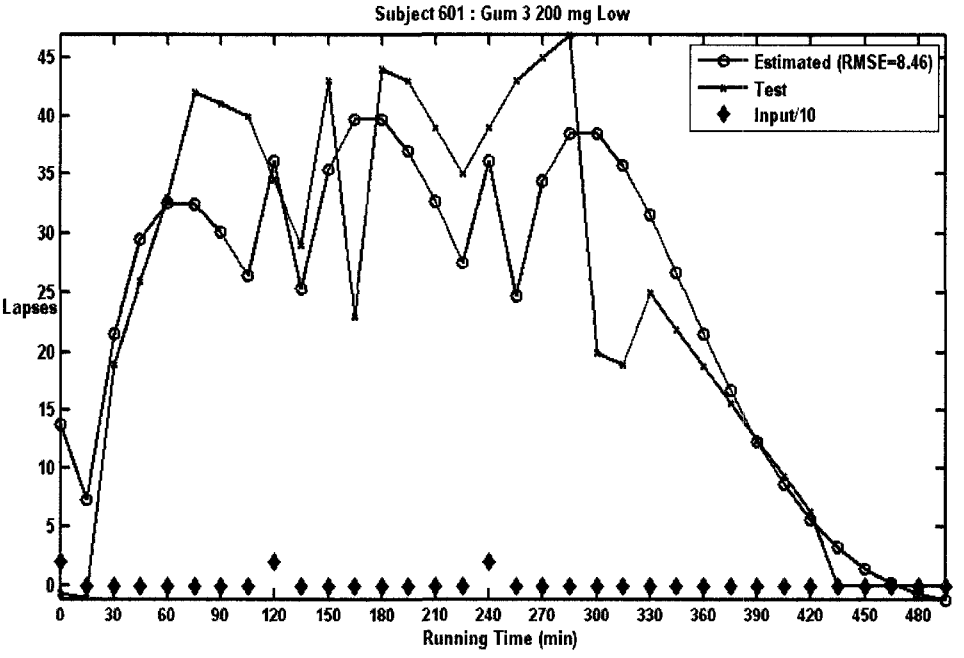

Figure 6.36: Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 601.

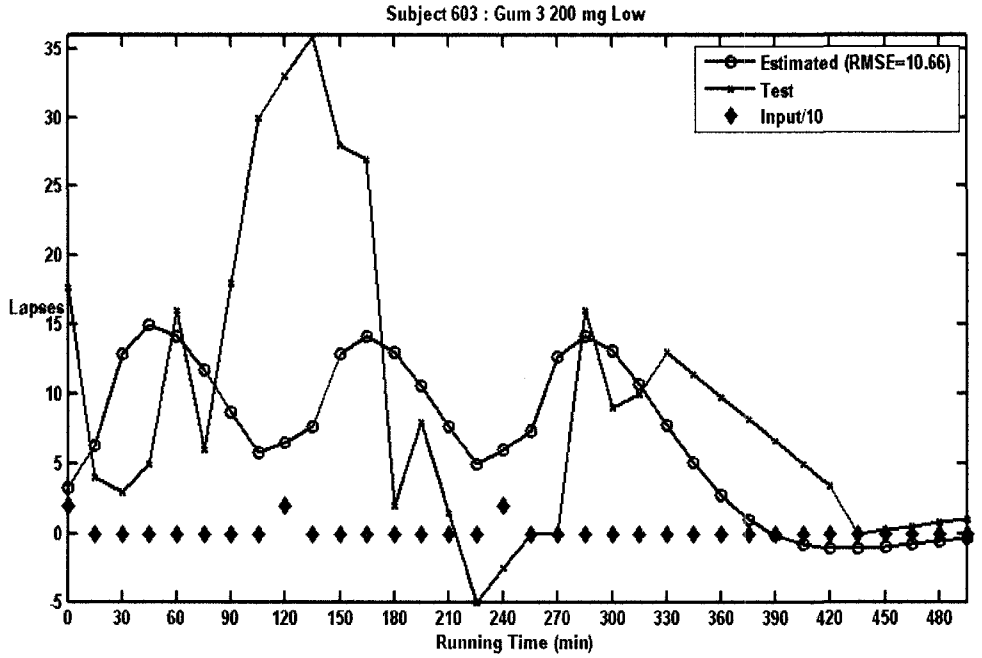

Figure 6.37: Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 603.

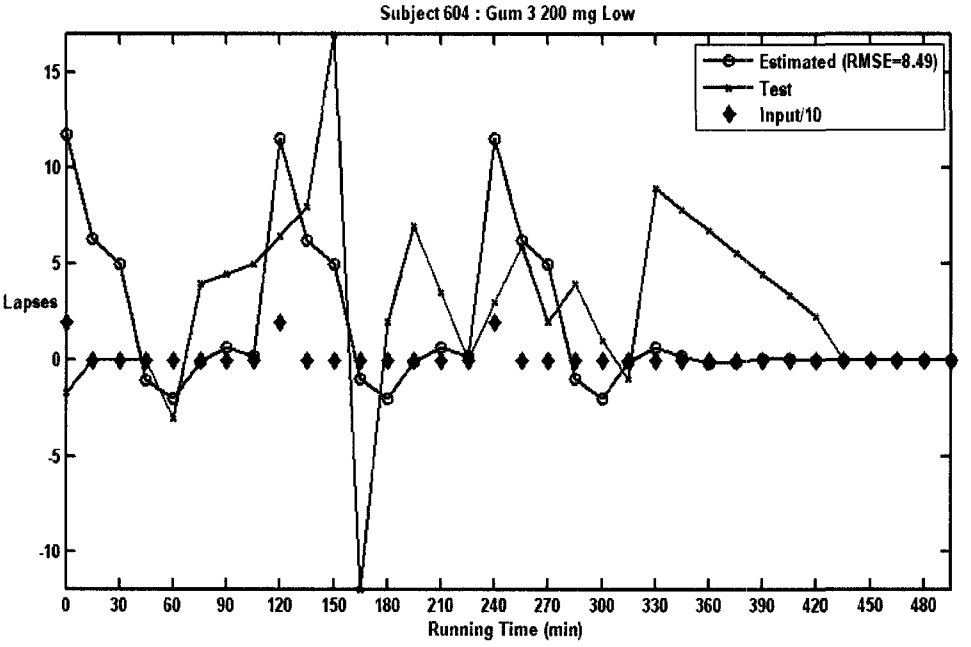

Figure 6.38: Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 604.

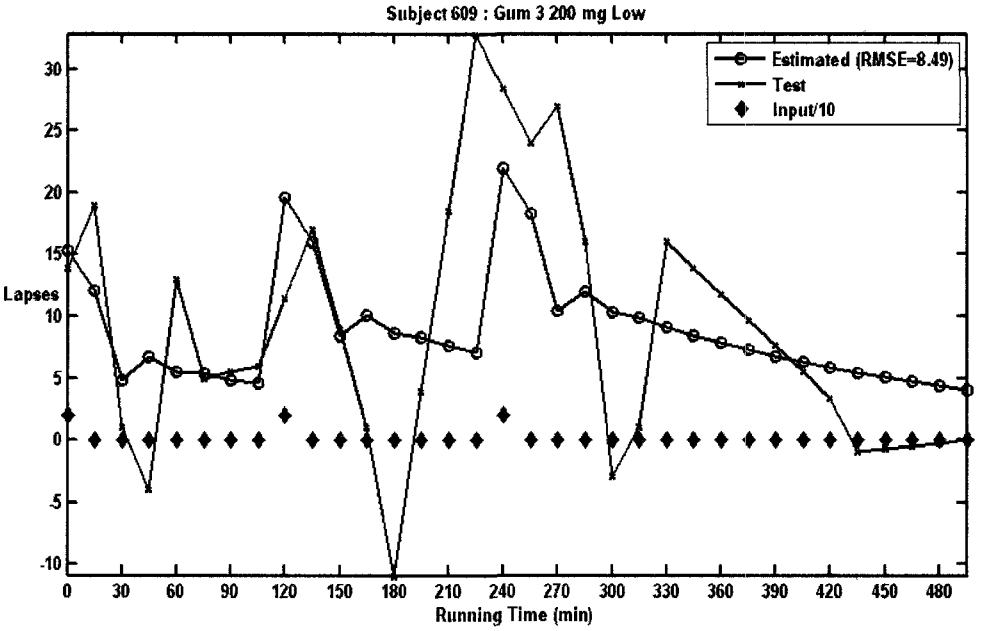

Figure 6.39: Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 609.

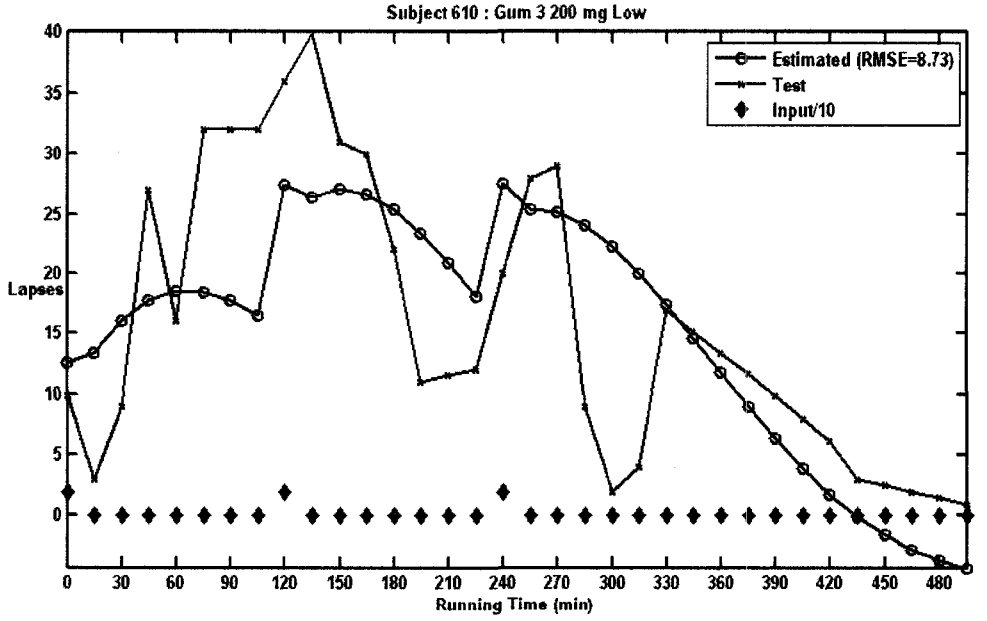

Figure 6.40: Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 610.

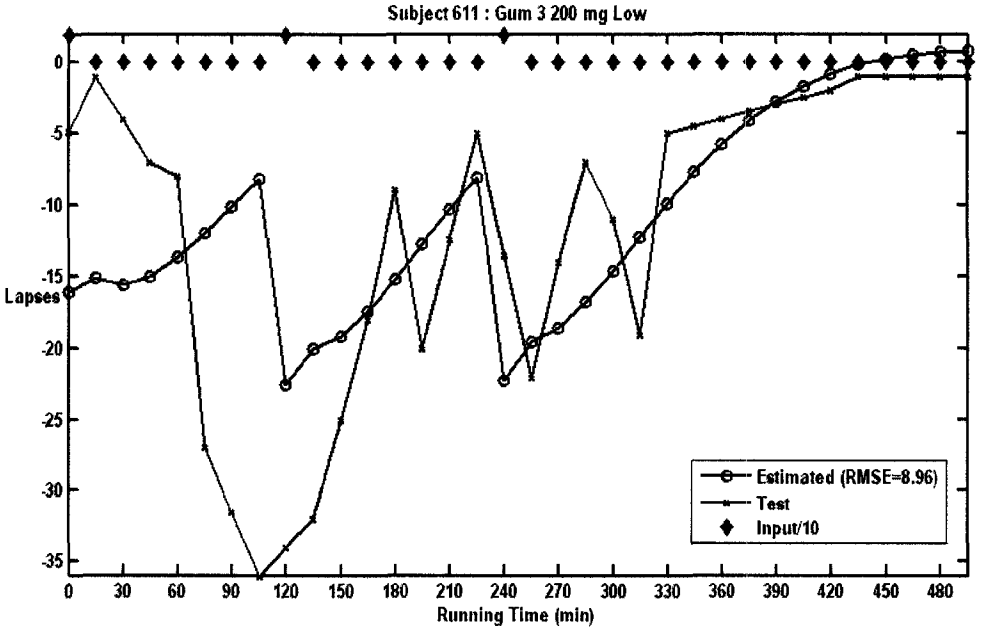

Figure 6.41: Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 611.

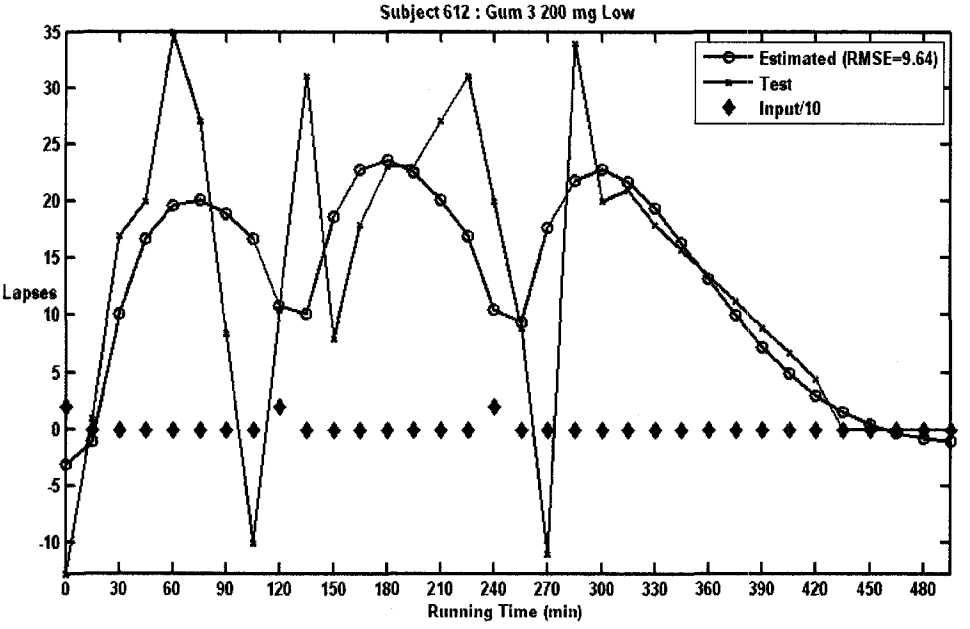

Figure 6.42: Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 612.

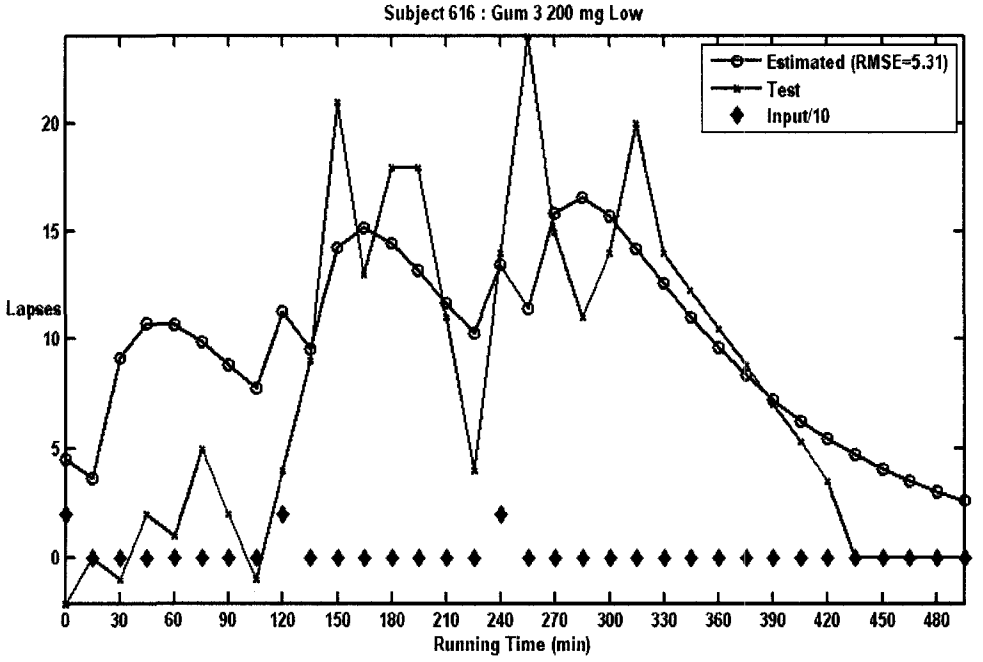

Figure 6.43: Individualized caffeine model developed for the differential effects between Gum 3 200 mg low-user data and placebo data for subject 616.

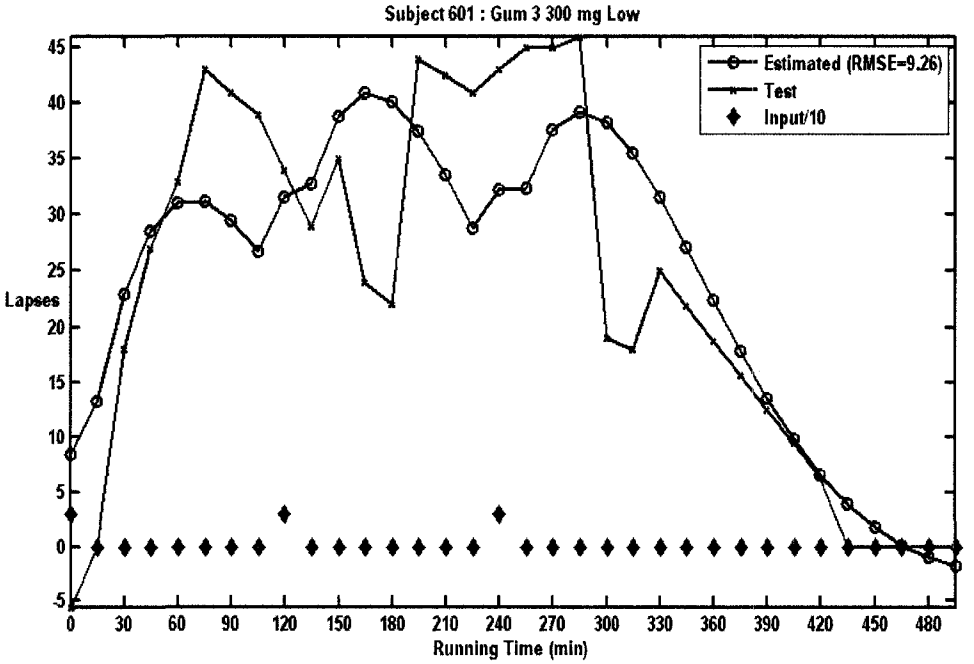

Figure 6.44: Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 601.

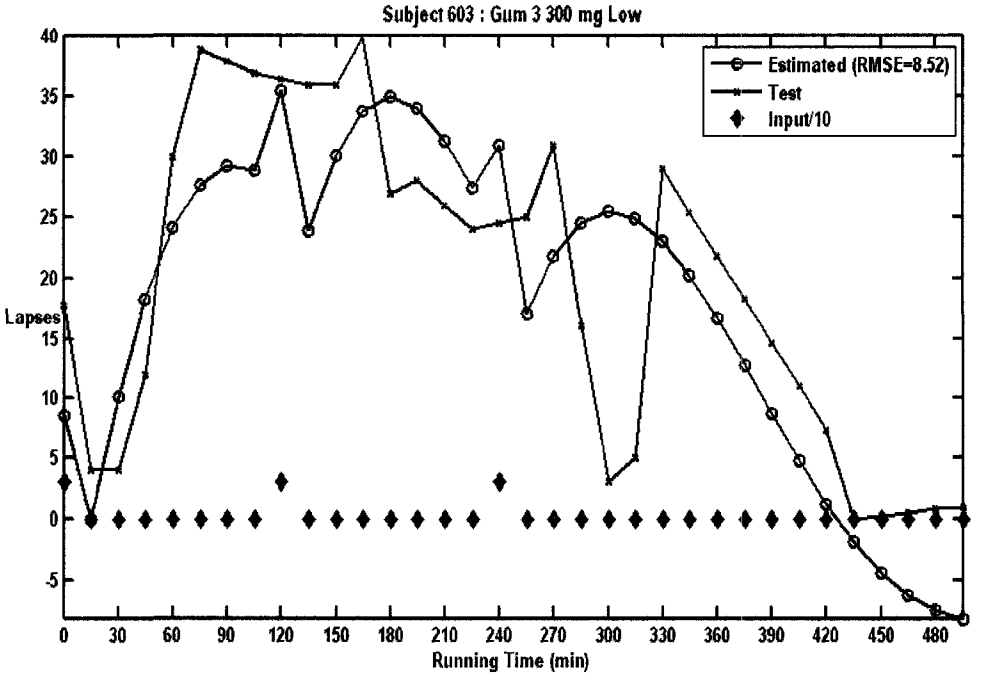

Figure 6.45: Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 603.

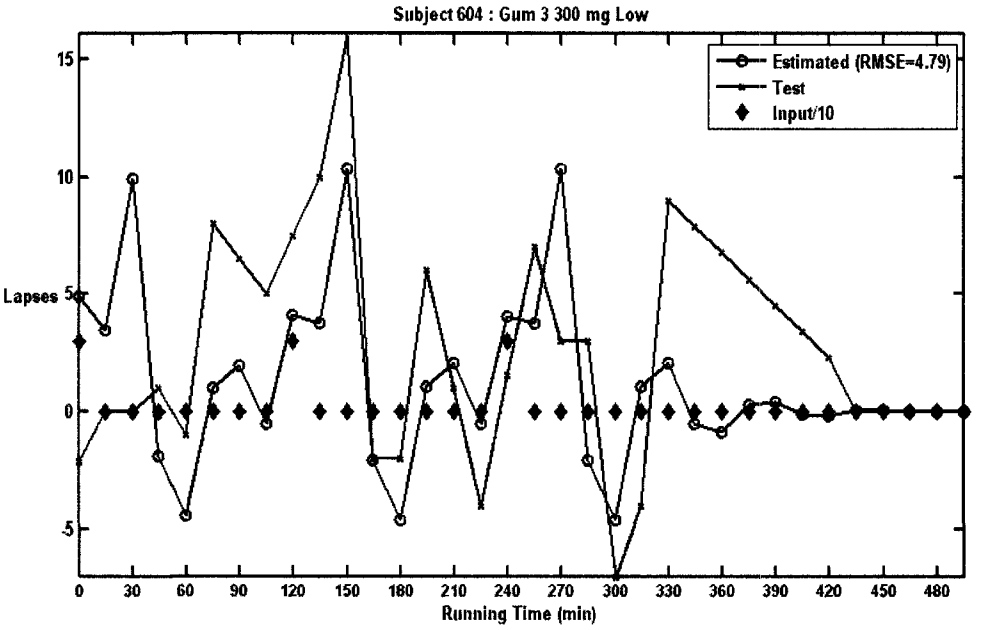

Figure 6.46: Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 604.

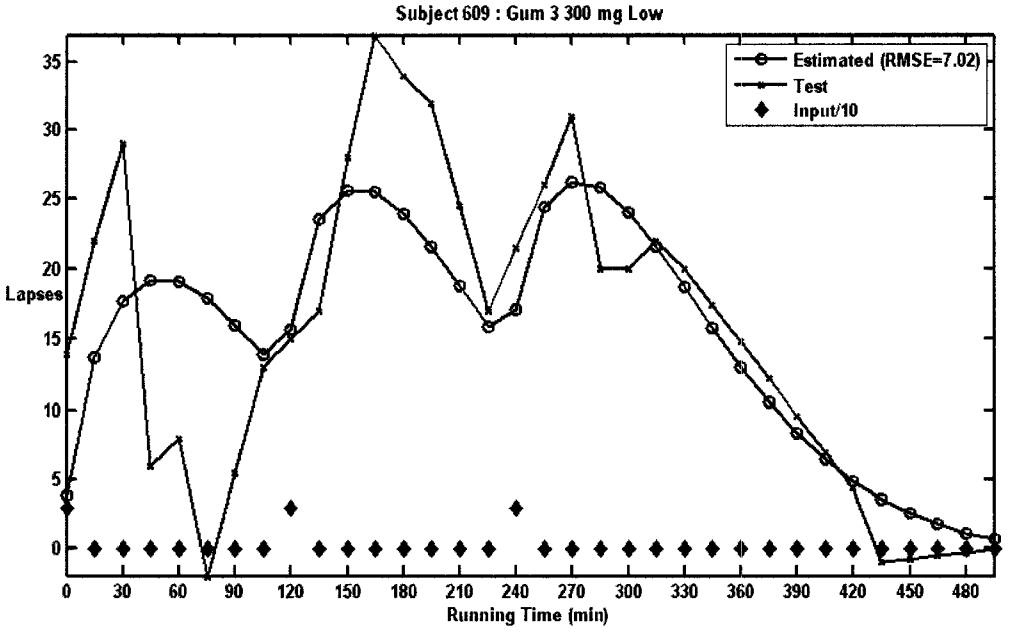

Figure 6.47: Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 609.

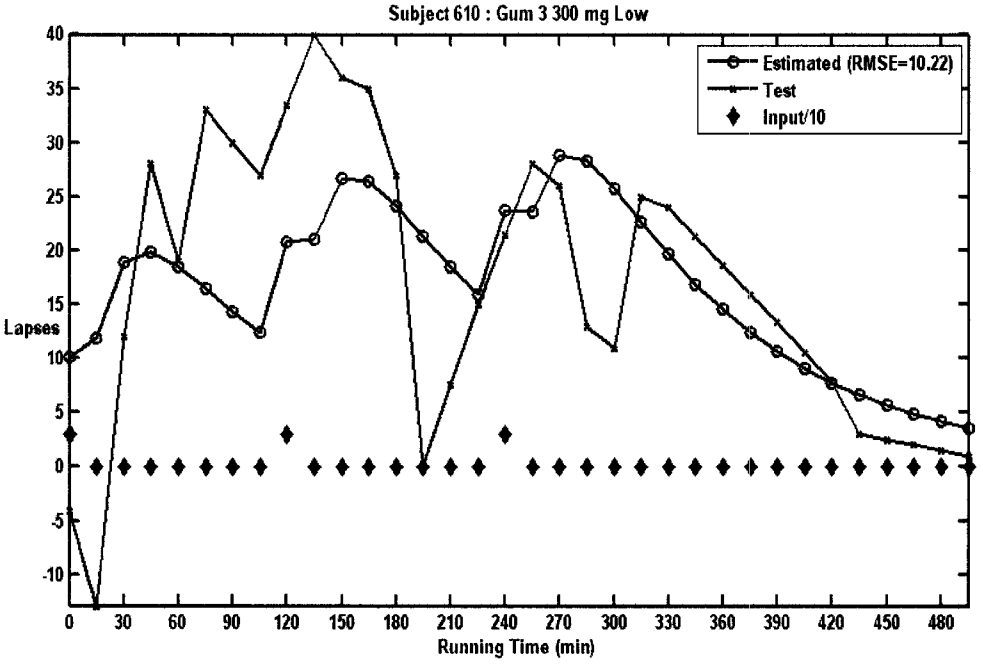

Figure 6.48: Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 610.

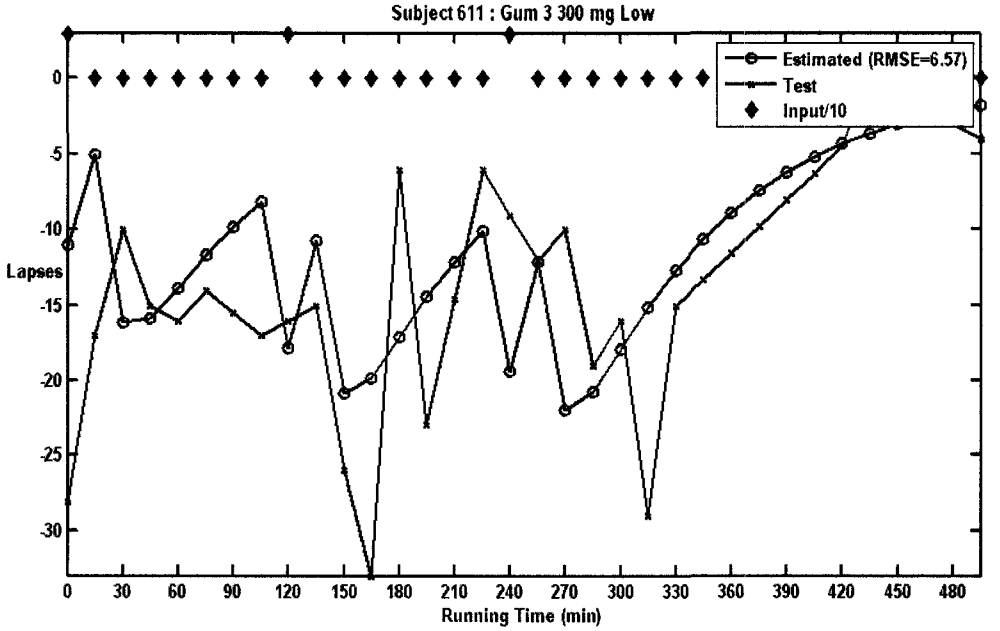

Figure 6.49: Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 611.

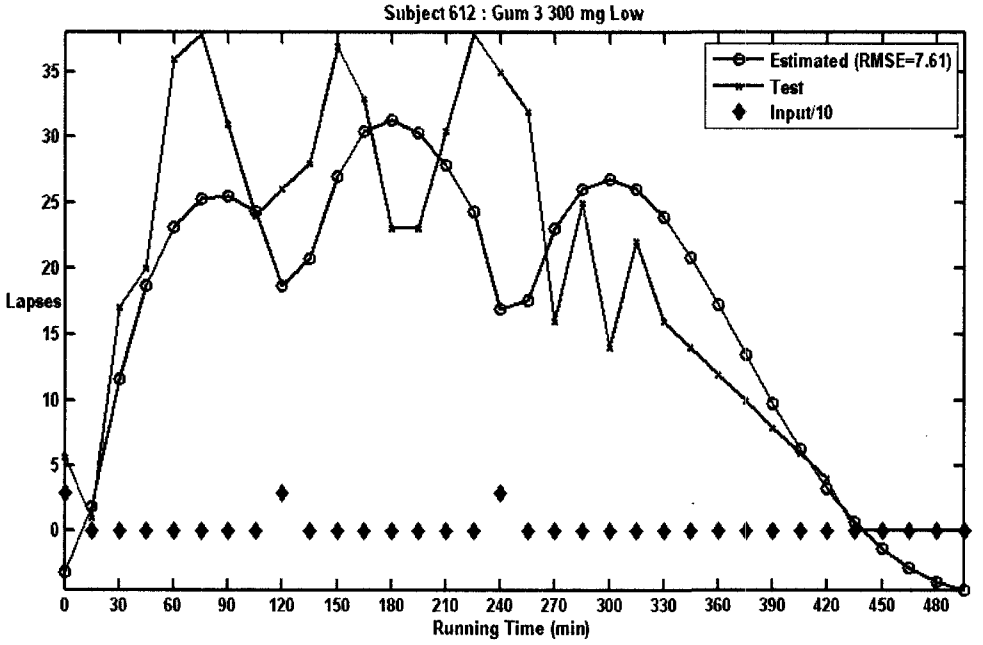

Figure 6.50: Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 612.

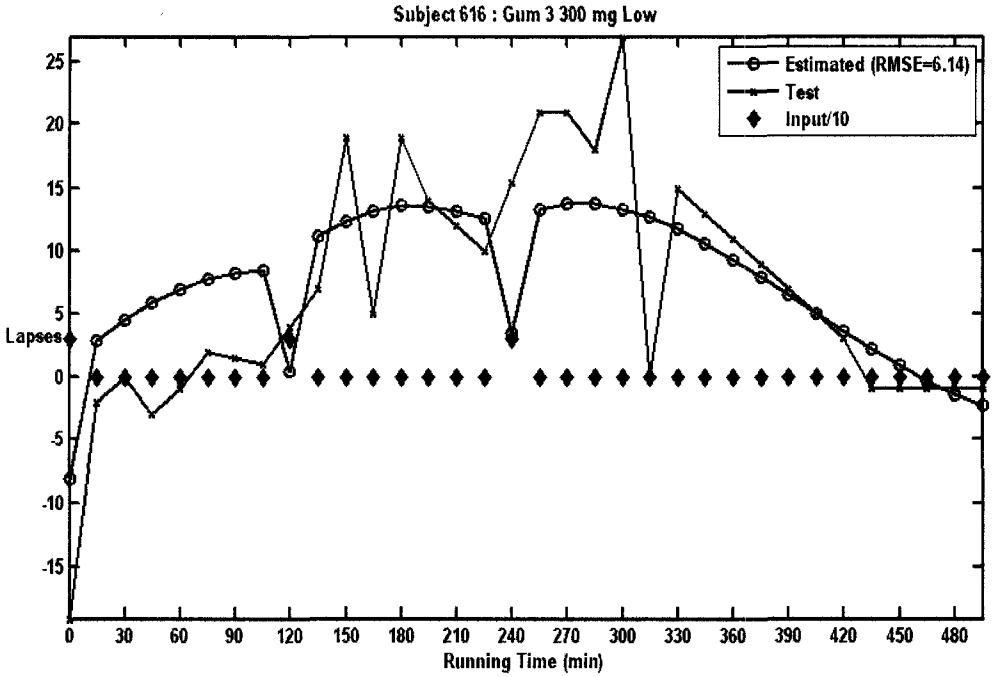

Figure 6.51: Individualized caffeine model developed for the differential effects between Gum 3 300 mg low-user data and placebo data for subject 616.

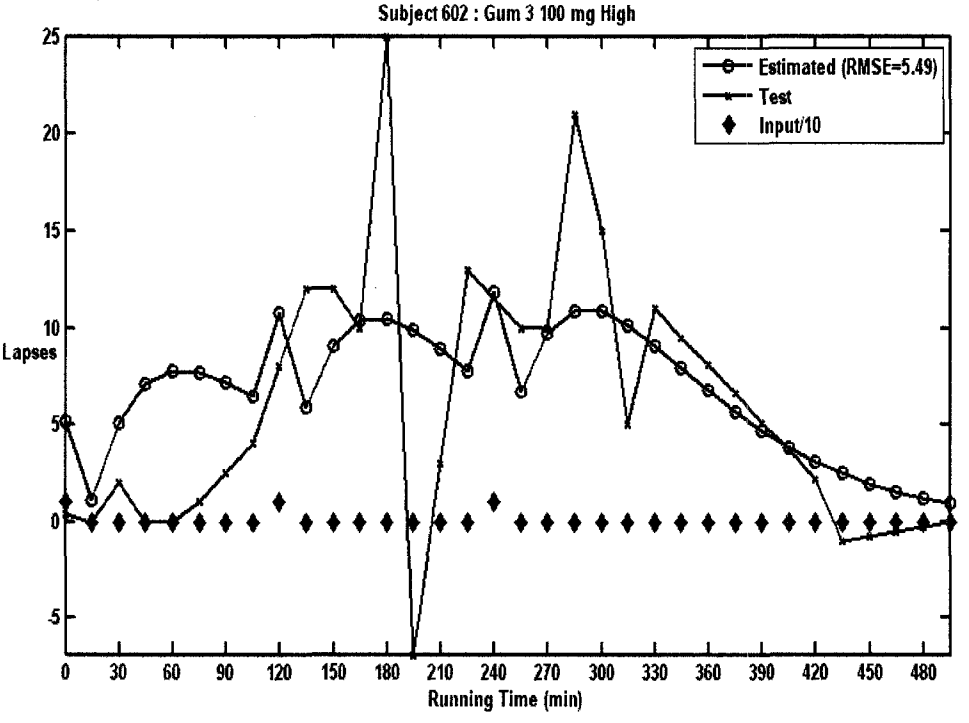

Figure 6.52: Individualized caffeine model developed for the differential effects between Gum 3 100 mg high-user data and placebo data for subject 602.

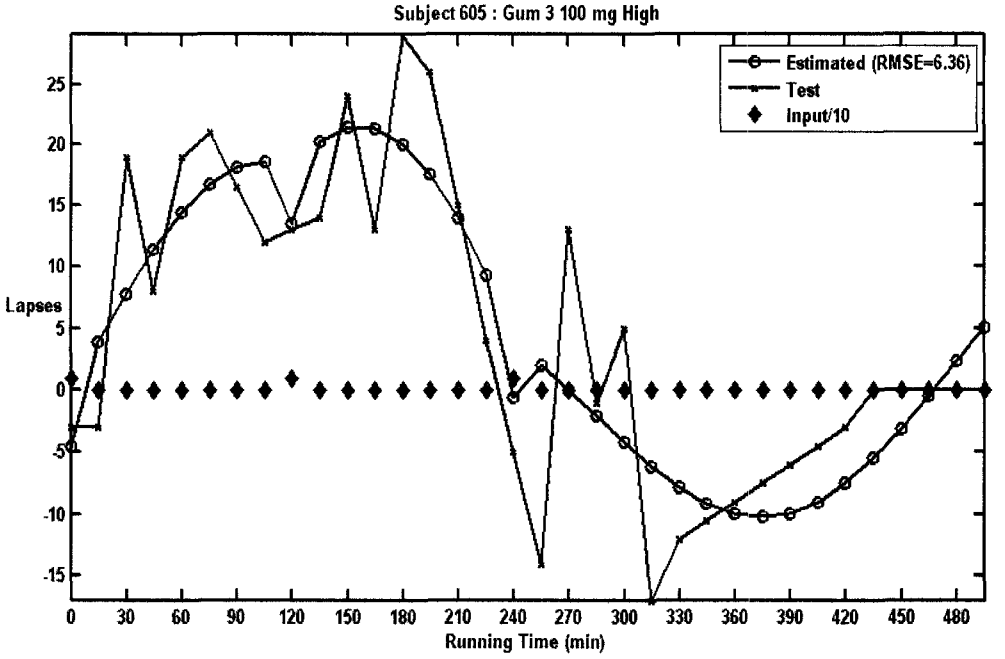

Figure 6.53: Individualized caffeine model developed for the differential effects between Gum 3 100 mg high-user data and placebo data for subject 605.

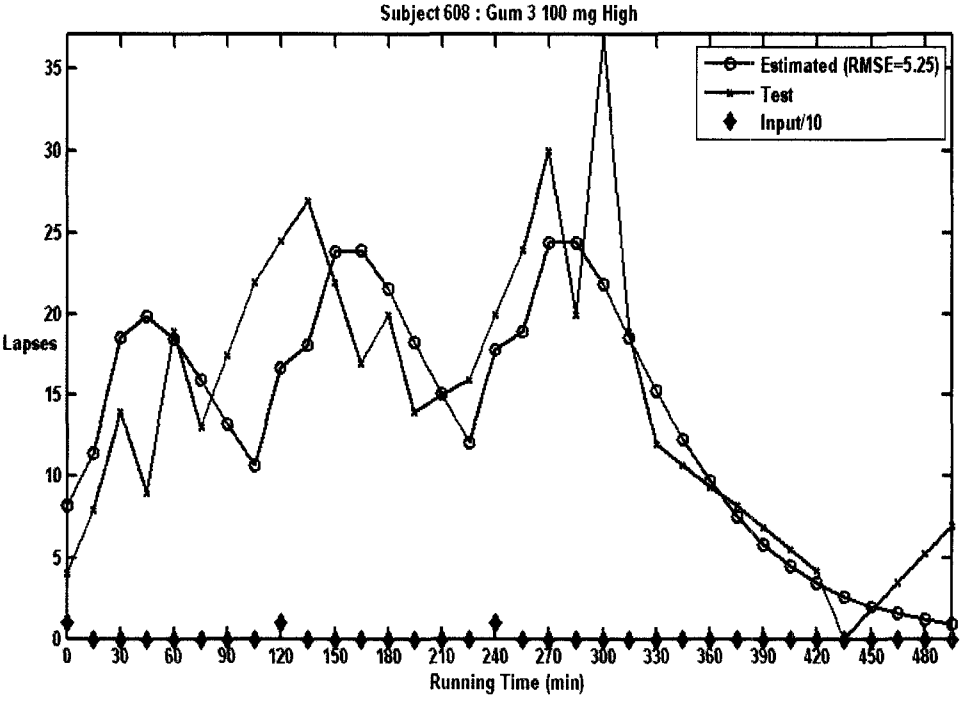

Figure 6.54: Individualized caffeine model developed for the differential effects between Gum 3 100 mg high-user data and placebo data for subject 608.

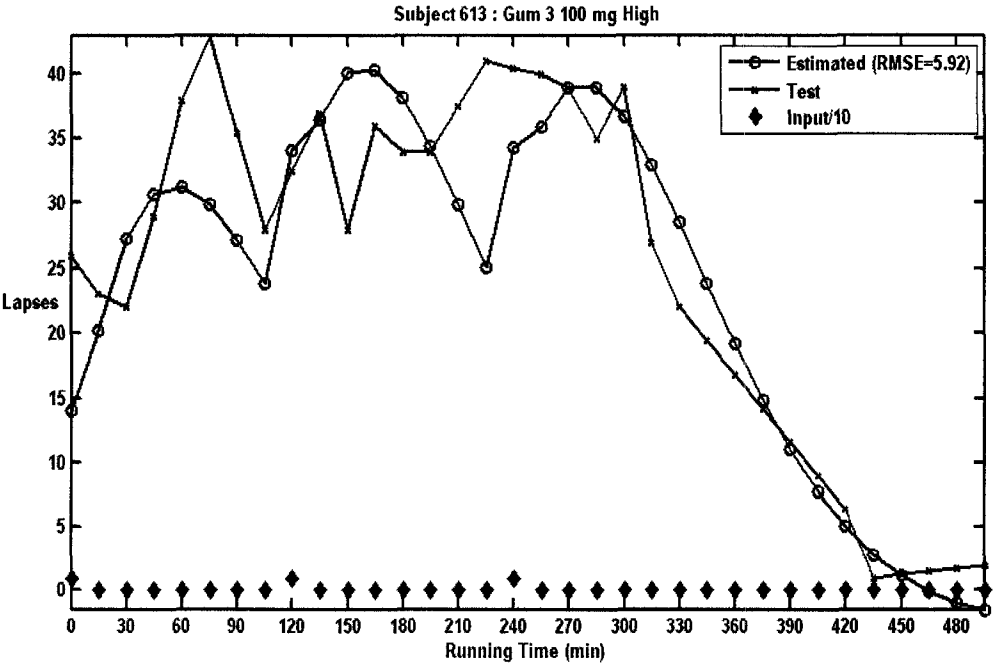

Figure 6.55: Individualized caffeine model developed for the differential effects between Gum 3 100 mg high-user data and placebo data for subject 613.

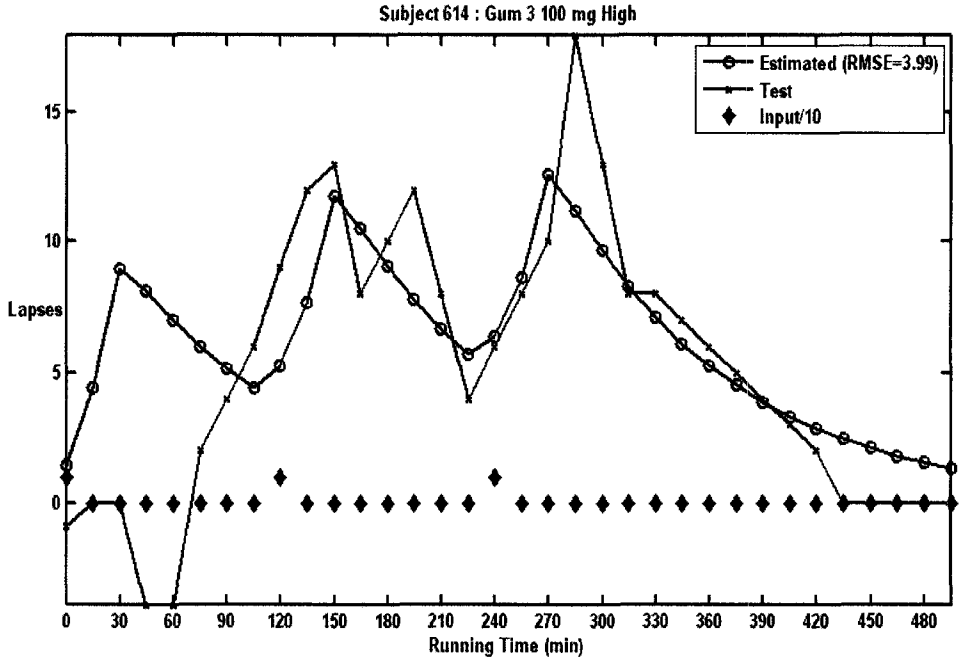

Figure 6.56: Individualized caffeine model developed for the differential effects between Gum 3 100 mg high-user data and placebo data for subject 614.

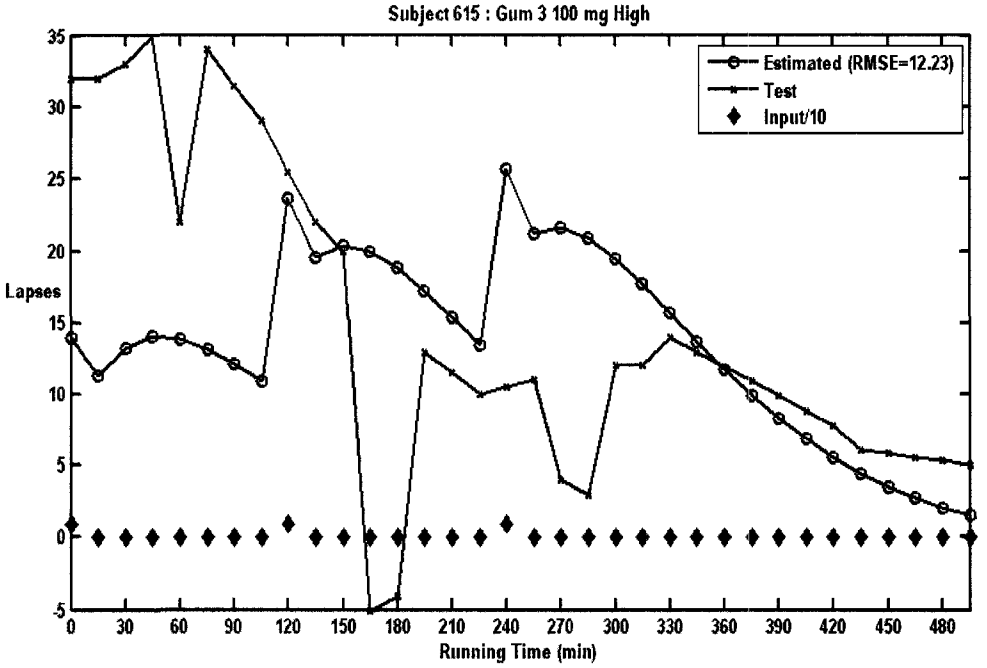

Figure 6.57: Individualized caffeine model developed for the differential effects between Gum 3 100 mg high-user data and placebo data for subject 615.

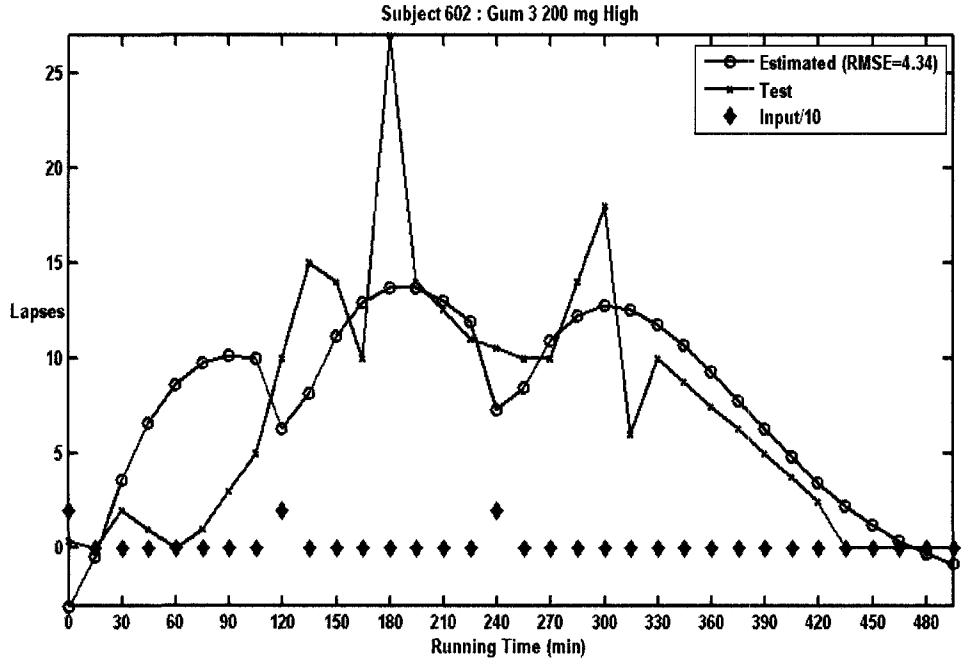

Figure 6.58: Individualized caffeine model developed for the differential effects between Gum 3 200 mg high-user data and placebo data for subject 602.

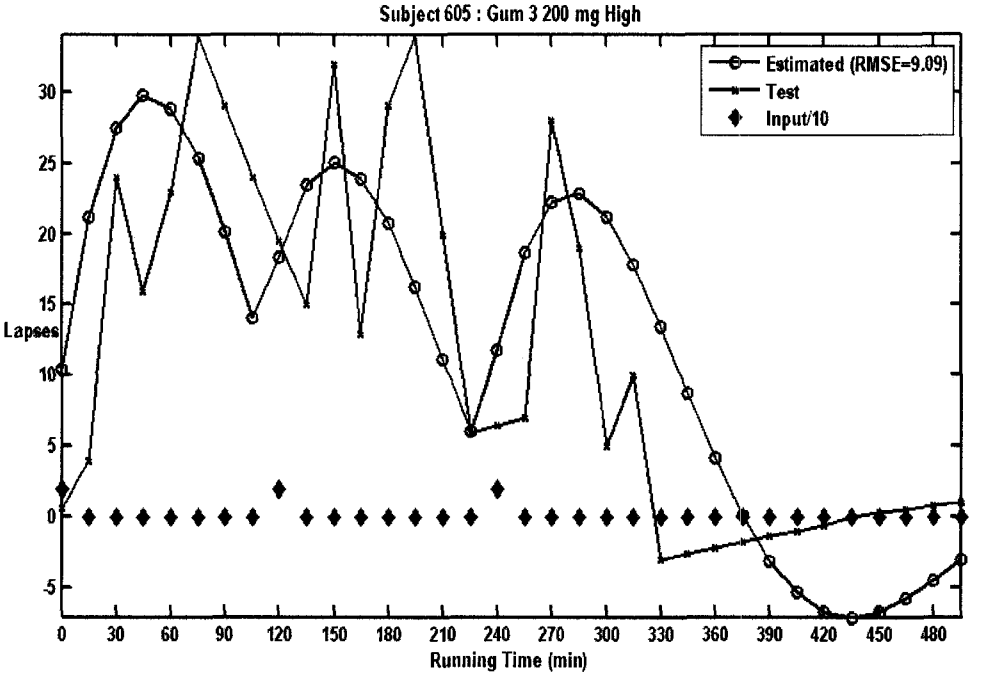

Figure 6.59: Individualized caffeine model developed for the differential effects between Gum 3 200 mg high-user data and placebo data for subject 605.

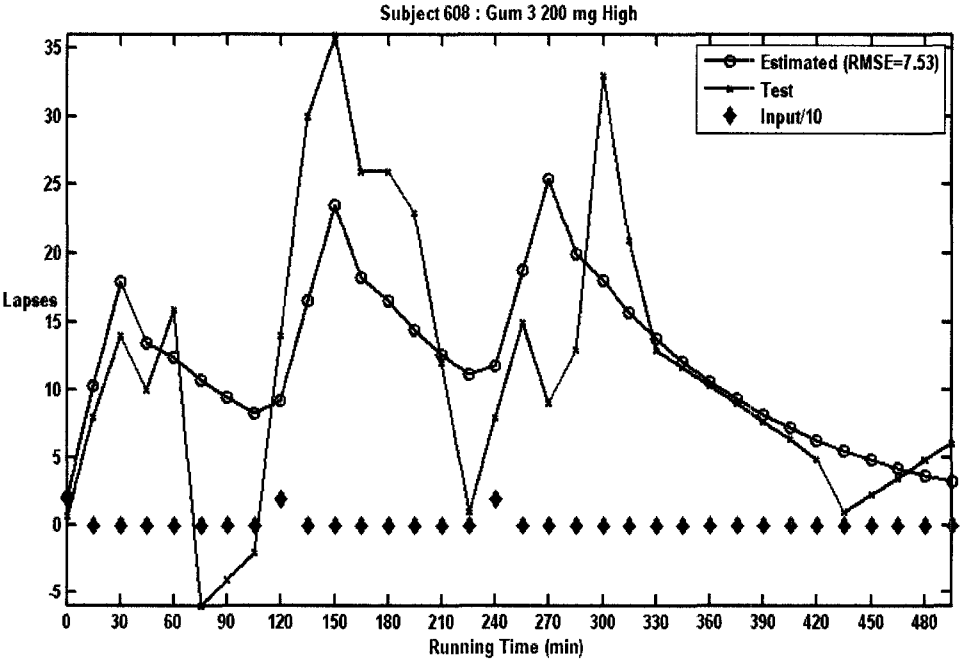

Figure 6.60: Individualized caffeine model developed for the differential effects between Gum 3 200 mg high-user data and placebo data for subject 608.

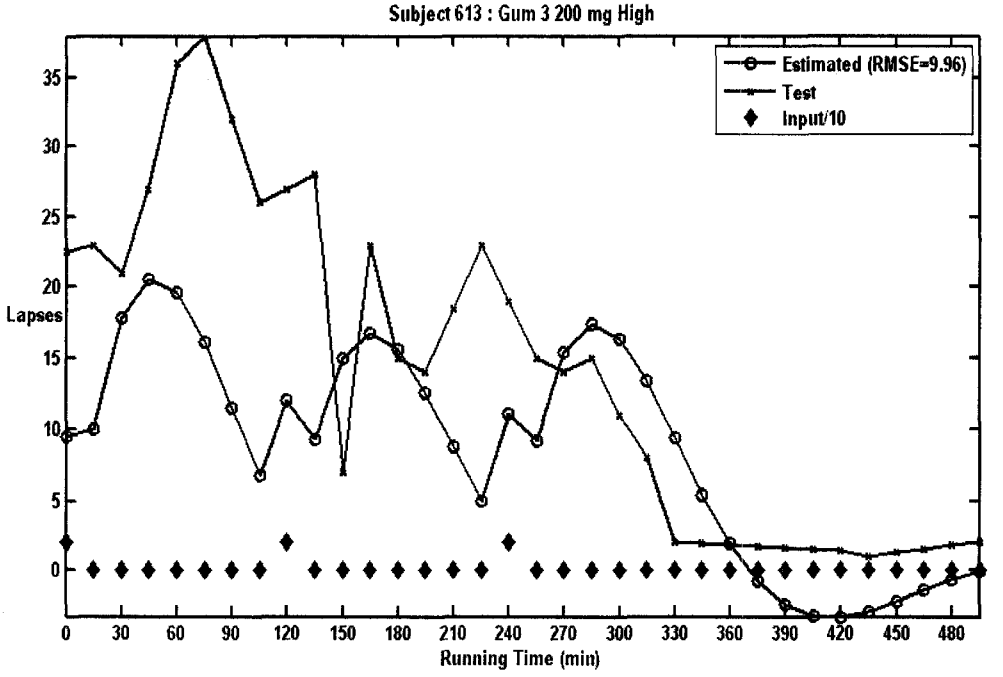

Figure 6.61: Individualized caffeine model developed for the differential effects between Gum 3 200 mg high-user data and placebo data for subject 613.

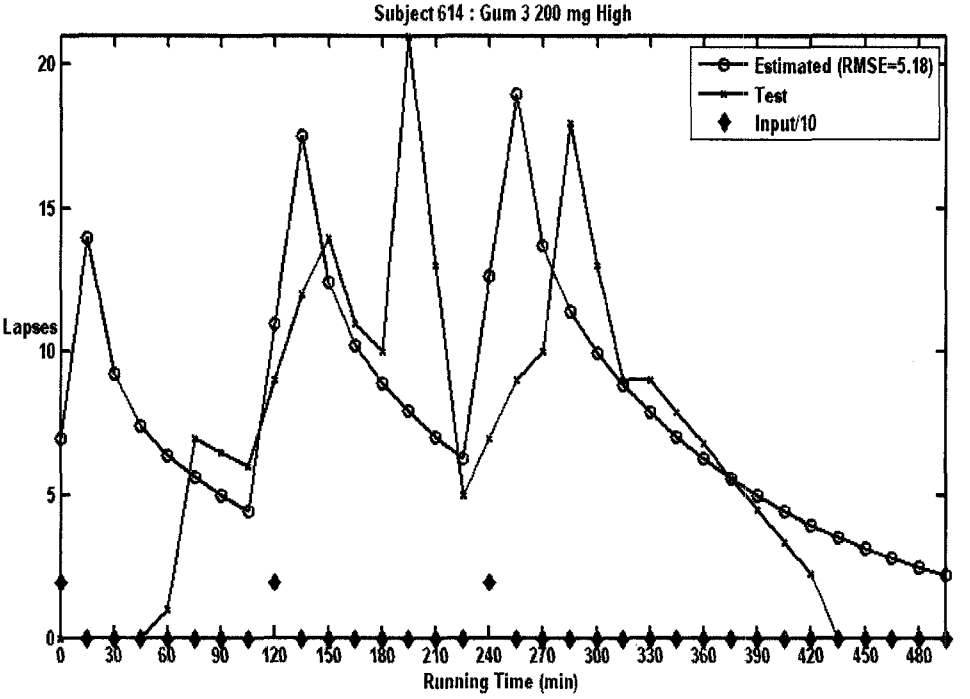

Figure 6.62: Individualized caffeine model developed for the differential effects between Gum 3 200 mg high-user data and placebo data for subject 614.

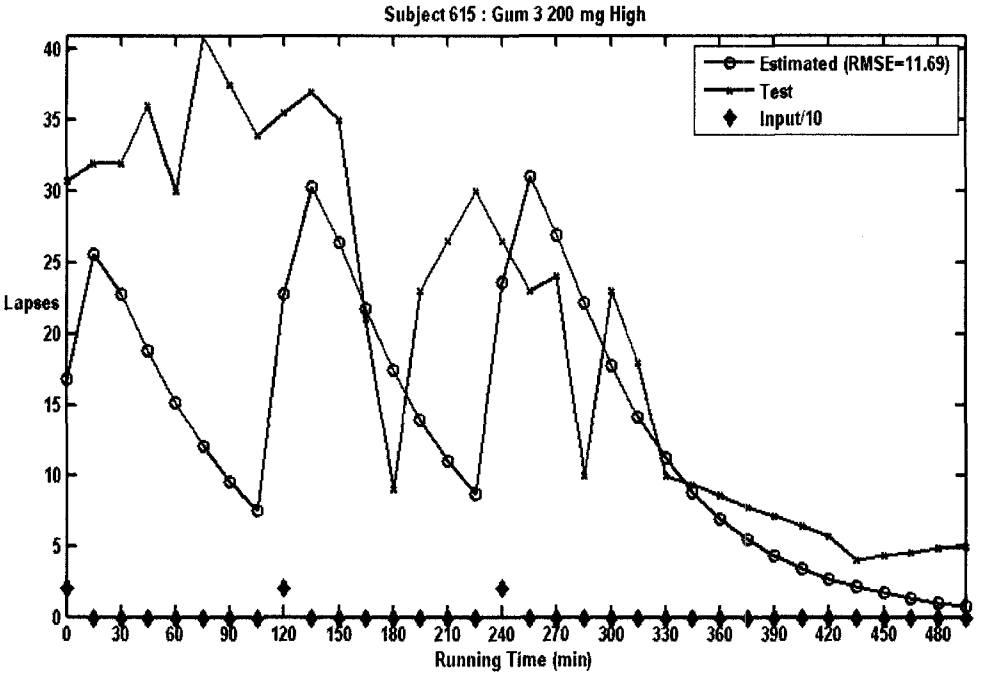

Figure 6.63: Individualized caffeine model developed for the differential effects between Gum 3 200 mg high-user data and placebo data for subject 615.

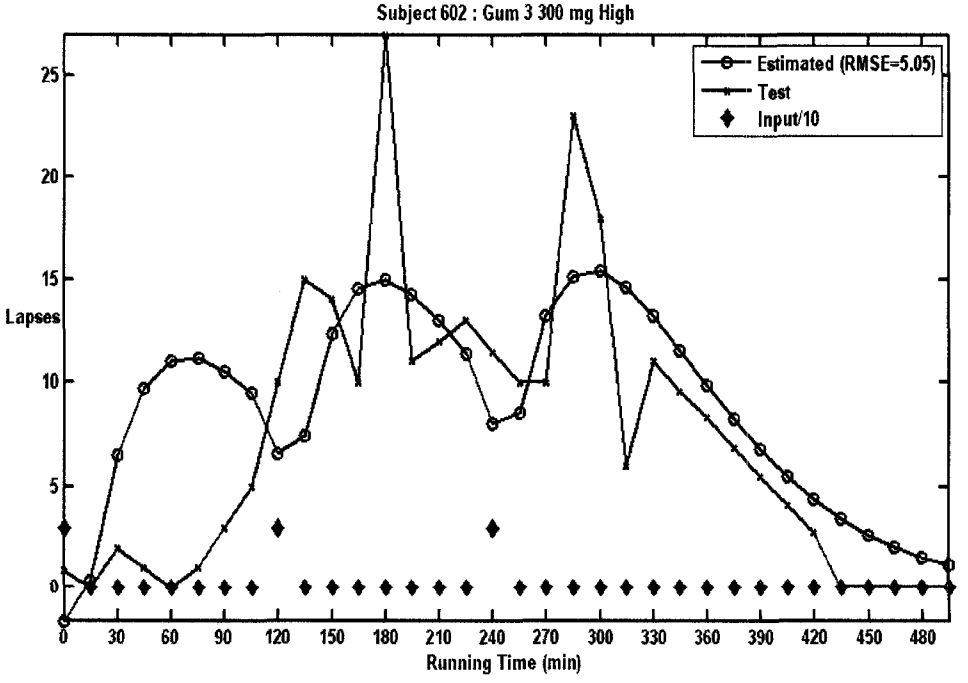

Figure 6.64: Individualized caffeine model developed for the differential effects between Gum 3 300 mg high-user data and placebo data for subject 602.

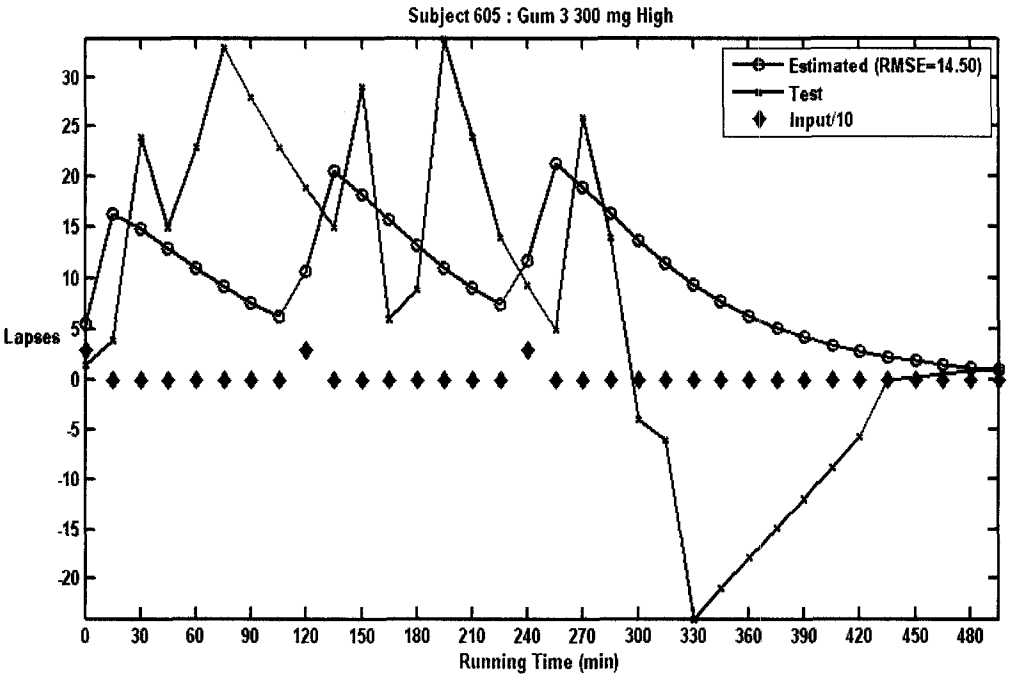

Figure 6.65: Individualized caffeine model developed for the differential effects between Gum 3 300 mg high-user data and placebo data for subject 605.

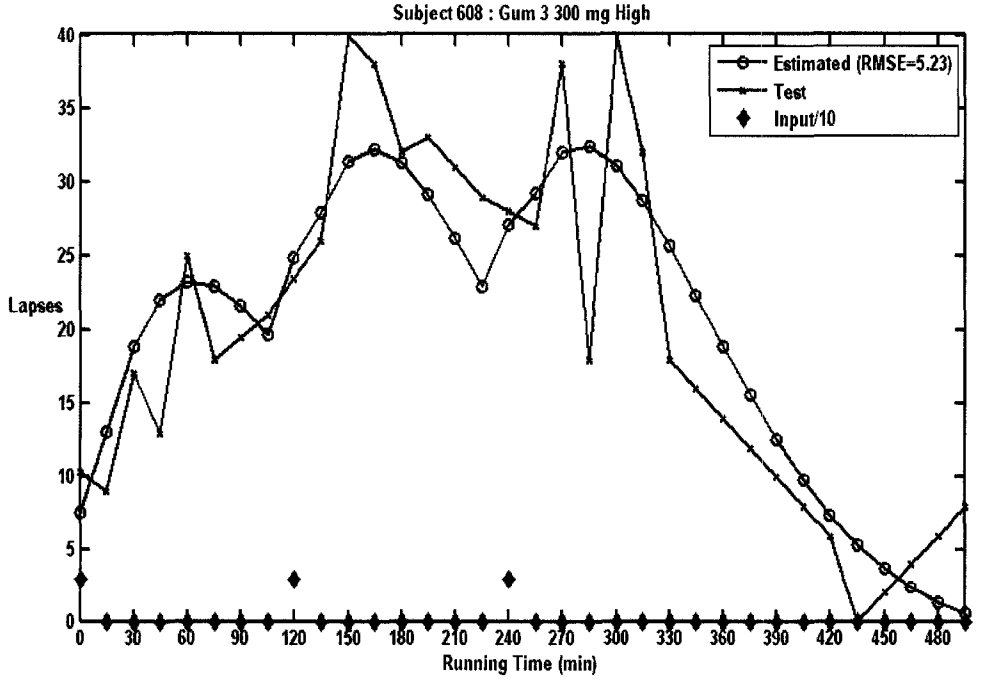

Figure 6.66: Individualized caffeine model developed for the differential effects between Gum 3 300 mg high-user data and placebo data for subject 608.

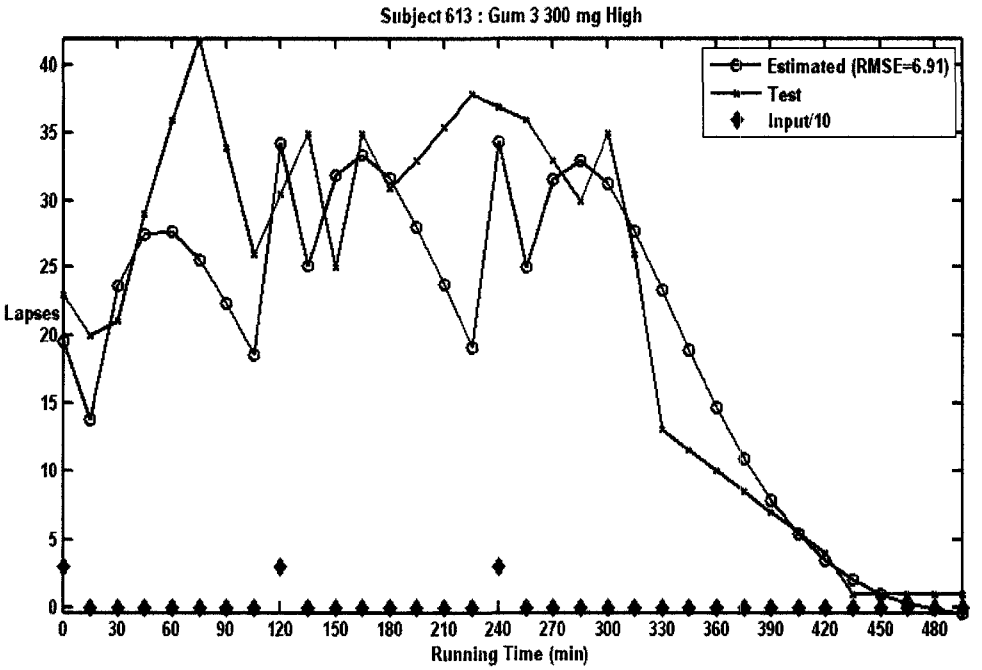

Figure 6.67: Individualized caffeine model developed for the differential effects between Gum 3 300 mg high-user data and placebo data for subject 613.

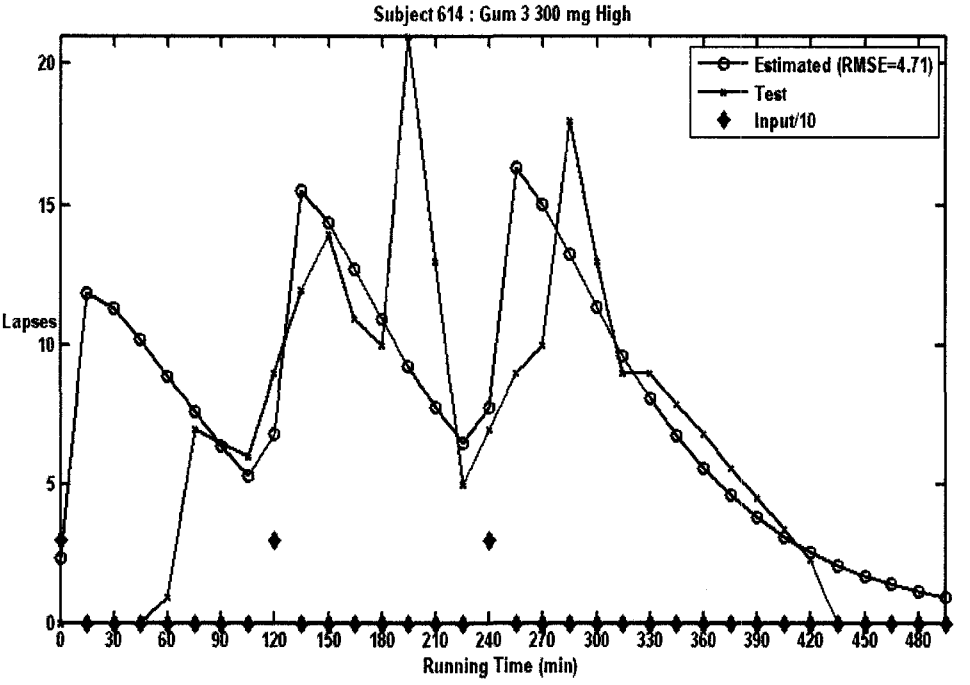

Figure 6.68: Individualized caffeine model developed for the differential effects between Gum 3 300 mg high-user data and placebo data for subject 614.

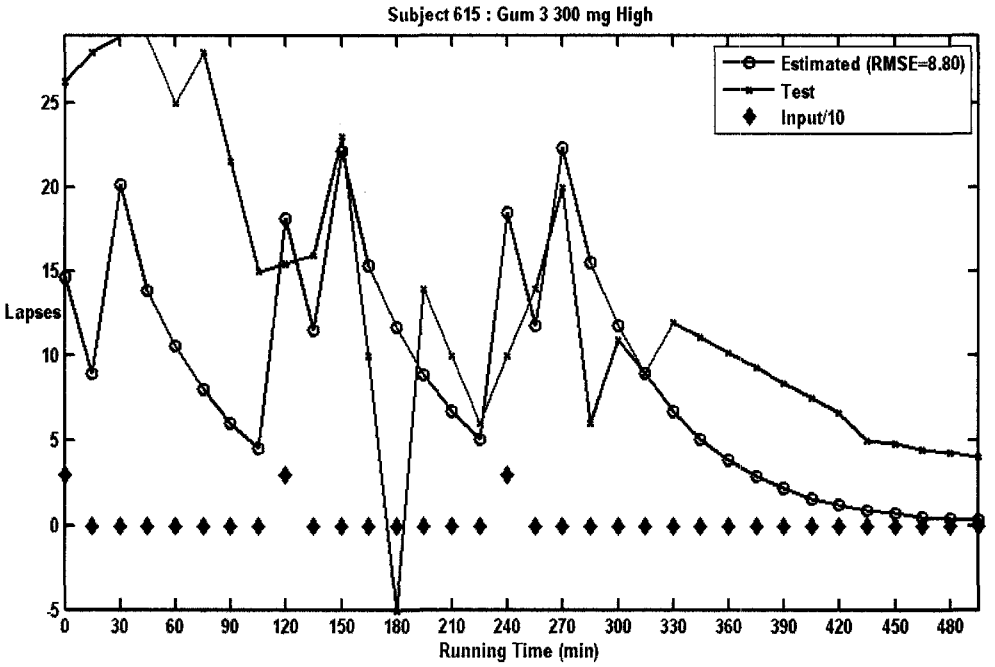

Figure 6.69: Individualized caffeine model developed for the differential effects between Gum 3 300 mg high-user data and placebo data for subject 615.

Table 6.1: Individualized Caffeine Model Coefficients Identified for Gum 2 Subjects

Subject	Dose (mg)	a_1	a_2	c_1	c_2	d_0	RMSE
504	50	-1.814	0.837	-0.260	0.730	0.275	2.19
506		-0.699	0.415	1.810	-1.113	0.129	3.26
511		-1.592	0.877	0.565	-1.016	0.087	8.36
513		-1.743	0.767	-0.203	0.779	-0.073	2.57
517		-1.952	1.024	-0.129	-0.683	-0.503	7.05
521		-1.174	0.260	-0.489	-2.456	-0.200	4.11
527		-1.735	0.780	0.233	0.405	0.309	2.96
535		-1.685	0.720	-0.096	0.882	0.319	2.54
539		-1.757	0.777	-0.410	0.824	0.079	2.64
AVG		-1.572	0.717	0.114	-0.183	0.047	3.96
507	100	-1.109	0.757	-0.516	0.542	-0.108	5.32
509		-1.437	0.480	0.118	0.335	0.344	2.62
524		-1.315	0.380	0.057	0.458	0.092	3.99
526		-1.636	0.667	0.055	0.368	0.111	1.73
529		-1.786	0.857	0.231	-0.038	0.049	4.24
536		-1.408	0.652	0.479	-1.222	-1.057	7.90
537		-1.801	1.020	-0.100	-0.285	0.360	7.70
543		-1.687	0.750	-0.001	0.624	0.194	3.60
545		-1.749	0.773	-0.031	0.366	-0.032	1.69
AVG		-1.548	0.704	0.033	0.128	-0.005	4.31
508	200	-1.529	0.582	0.252	0.011	0.038	2.31
510		-1.495	0.499	-0.418	0.467	0.176	4.46
515		-1.678	0.707	0.006	0.196	0.085	1.70
522		-0.017	-0.626	-0.845	-0.290	0.150	7.91
528		-1.706	0.736	0.078	0.121	-0.008	1.88
531		-1.769	0.794	-0.005	0.163	-0.061	1.87
533		-1.786	0.808	-0.056	0.199	-0.007	1.65
540		-1.716	0.748	0.023	0.175	0.056	1.93
541		-1.745	0.771	0.025	0.148	0.023	1.58
AVG		-1.493	0.558	-0.104	0.132	0.050	2.81

Table 6.2: Individualized Caffeine Model Coefficients Identified for Gum 3 Low-users

Subject	Dose (mg)	a_1	a_2	c_1	c_2	d_0	RMSE
601 L	100	-1.874	0.943	2.860	-1.853	0.048	12.86
603 L		-1.122	0.311	1.388	0.712	1.194	7.87
604 L		-1.703	0.784	-0.161	0.307	0.239	4.06
609 L		-0.549	-0.341	-0.553	1.557	1.237	8.77
610 L		-1.800	0.825	-0.688	0.999	0.974	10.50
611 L		-1.897	0.946	0.869	-0.694	-0.206	4.54
612 L		-1.695	0.738	-0.985	1.817	0.249	9.25
616 L		-1.723	0.764	0.567	-0.018	0.187	5.71
AVG		-1.545	0.621	0.412	0.353	0.490	7.94
601 L	200	-1.589	0.658	0.494	0.369	0.693	8.46
603 L		-1.453	0.589	0.182	0.317	0.164	10.66
604 L		-0.234	0.348	0.176	0.318	0.589	5.52
609 L		-0.574	-0.329	-0.107	0.607	0.769	8.49
610 L		-1.793	0.829	-0.393	0.668	0.628	8.73
611 L		-1.622	0.681	0.447	-0.754	-0.803	8.96
612 L		-1.578	0.653	0.583	-0.047	-0.155	9.64
616 L		-1.338	0.410	0.214	0.182	0.226	5.31
AVG		-1.273	0.480	0.199	0.208	0.264	8.22
601 L	300	-1.660	0.715	0.031	0.442	0.279	9.26
603 L		-1.792	0.847	0.340	0.000	0.285	8.52
604 L		0.034	0.450	0.336	0.115	0.164	4.79
609 L		-1.578	0.636	-0.133	0.459	0.129	7.02
610 L		-1.275	0.360	0.124	0.398	0.338	10.22
611 L		-1.041	0.171	-0.362	-0.167	-0.366	6.57
612 L		-1.727	0.784	0.280	0.063	-0.107	7.61
616 L		-1.869	0.895	-0.026	0.095	-0.271	6.14
AVG		-1.364	0.607	0.074	0.176	0.056	7.53

Table 6.3: Individualized Caffeine Model Coefficients Identified for Gum 3 High-users

Subject	Dose (mg)	a_1	a_2	c_1	c_2	d_0	RMSE
602 H	100	-1.515	0.578	0.344	0.111	0.521	5.49
605 H		-1.983	1.041	0.002	0.391	-0.456	6.36
608 H		-1.341	0.442	0.327	1.144	0.820	5.25
613 H		-1.637	0.693	-0.568	2.016	1.406	5.92
614 H		-0.942	0.071	0.480	0.440	0.145	3.99
615 H		-1.620	0.665	-0.498	1.129	1.402	12.23
AVG		-1.506	0.582	0.014	0.872	0.640	6.54
602 H	200	-1.727	0.773	0.219	-0.022	-0.159	4.34
605 H		-1.699	0.794	-0.428	1.060	0.520	9.09
608 H		-0.619	-0.226	0.582	0.513	0.102	7.53
613 H		-1.542	0.683	0.117	0.502	0.474	9.96
614 H		-1.151	0.231	-0.344	0.699	0.350	5.18
615 H		-1.137	0.275	-0.318	1.279	0.840	11.69
AVG		-1.313	0.422	-0.029	0.672	0.355	7.97
602 H	300	-1.535	0.597	0.197	0.012	-0.057	5.05
605 H		-1.377	0.459	-0.257	0.547	0.189	14.50
608 H		-1.651	0.699	-0.089	0.435	0.252	5.23
613 H		-1.520	0.600	0.085	0.462	0.650	6.91
614 H		-1.375	0.454	-0.165	0.396	0.079	4.71
615 H		-0.658	-0.073	0.476	0.298	0.490	8.80
AVG		-1.353	0.456	0.041	0.358	0.267	7.53

Table 6.4: Individualized Caffeine Model Coefficients Statistics

Parameters	GUM 2		GUM 3	
	Mean	STD	Mean	STD
a_1	-1.538	0.405	-1.392	0.471
a_2	0.660	0.312	0.534	0.337
c_1	0.014	0.469	0.134	0.623
c_2	0.026	0.755	0.412	0.666
d_0	0.031	0.283	0.335	0.487

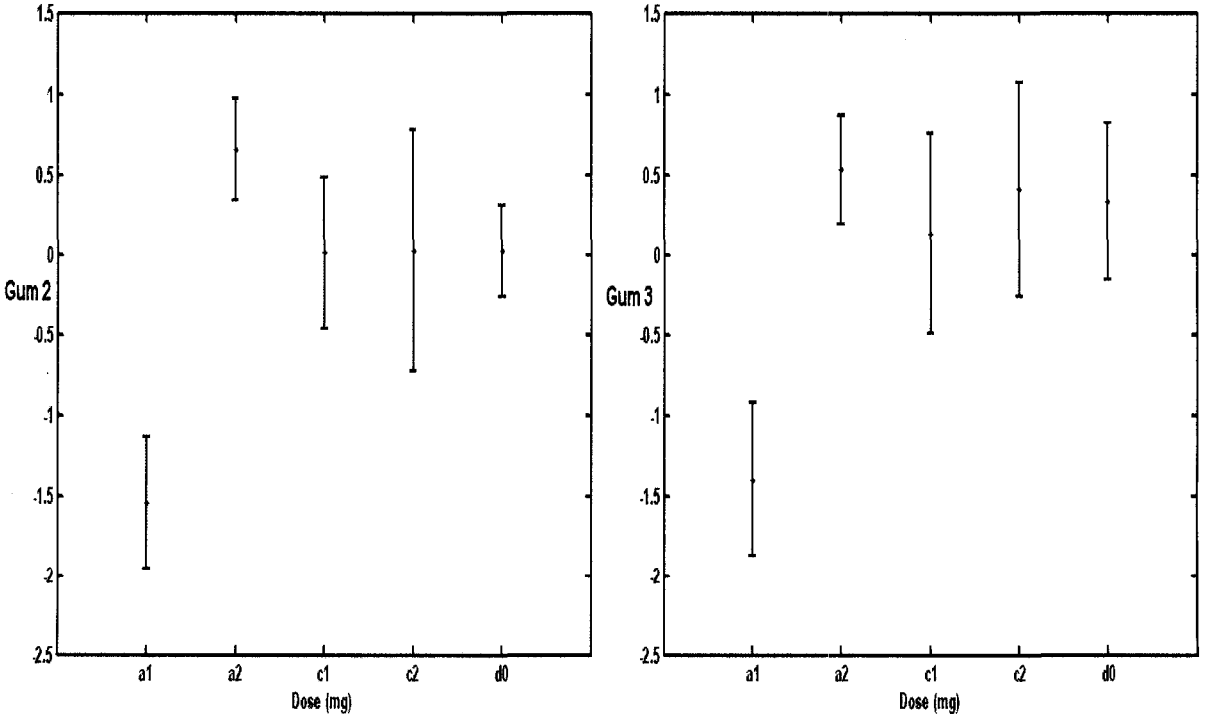

Figure 6.70: Individualized Caffeine Model Coefficients Statistics

Table 6.5: Individualized Caffeine Model Coefficients Statistics for Dose Effect

Parameters	50mg		100mg		200mg		300mg	
	Mean	STD	Mean	STD	Mean	STD	Mean	STD
a_1	-1.572	0.392	-1.536	0.345	-1.369	0.516	-1.359	0.512
a_2	0.717	0.236	0.643	0.316	0.495	0.396	0.542	0.266
c_1	0.114	0.714	0.160	0.797	0.021	0.358	0.060	0.247
c_2	-0.183	1.185	0.400	0.890	0.299	0.423	0.254	0.226
d_0	0.047	0.270	0.335	0.606	0.204	0.371	0.147	0.278

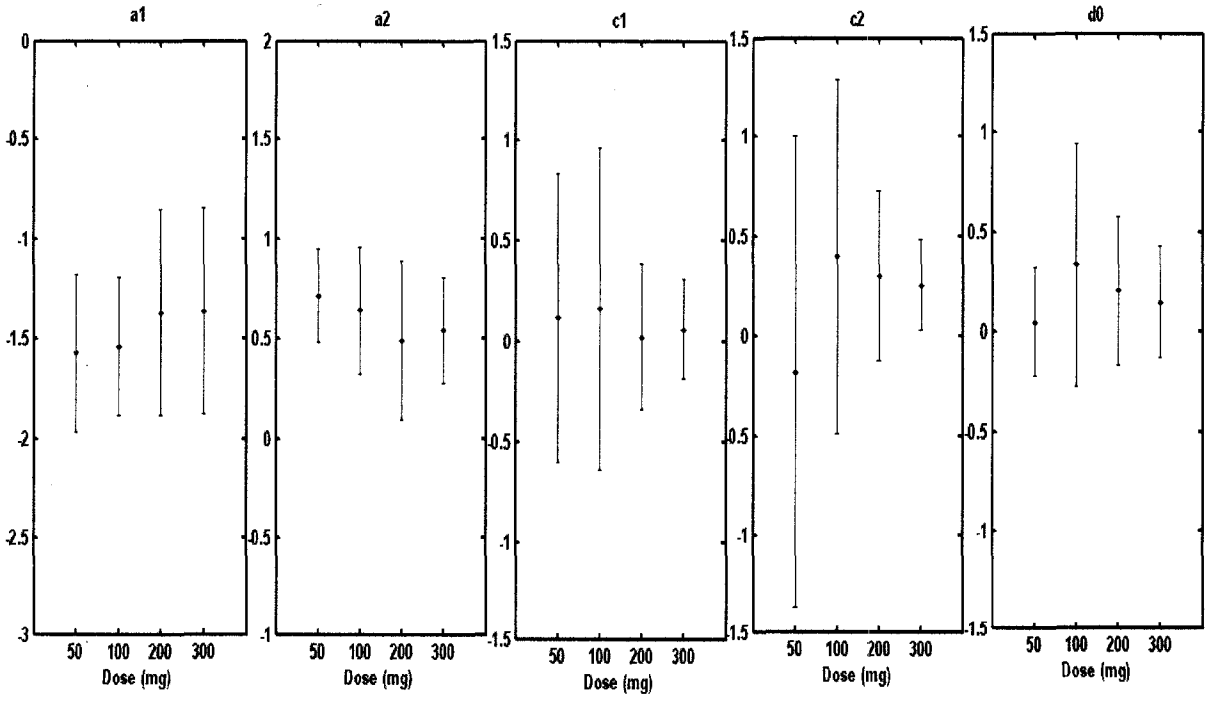

Figure 6.71: Individualized Caffeine Model Coefficients Statistics for Dose Effect

Table 6.6: Individualized Caffeine Model Coefficients Statistics for Habitual Effect

Parameters	Gum 3 Low		Gum 3 High	
	Mean	STD	Mean	STD
a_1	-1.394	0.544	-1.390	0.366
a_2	0.569	0.349	0.486	0.324
c_1	0.228	0.759	0.009	0.360
c_2	0.245	0.727	0.634	0.514
d_0	0.270	0.487	0.420	0.489

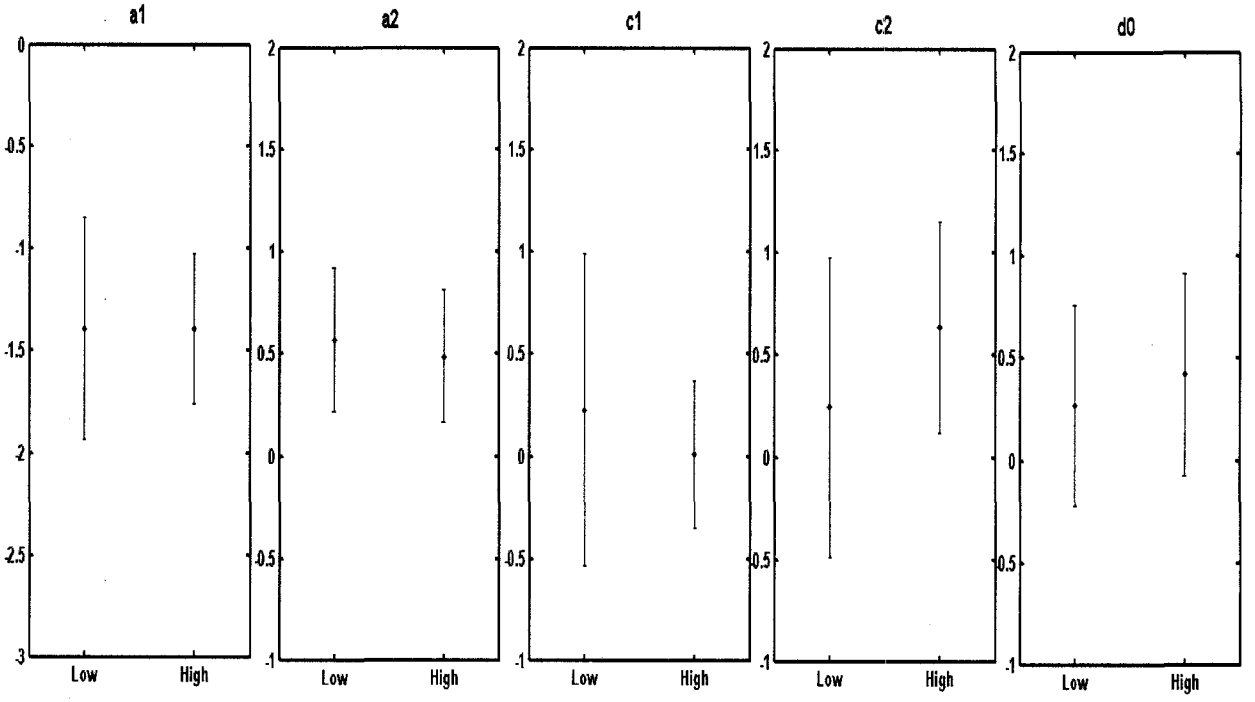

Figure 72: Individualized Caffeine Model Coefficients Statistics for Habitual Effect

6.2 Effect of Caffeine Dosage on Individual Subject Performance

In this section, we study the effect of caffeine dosage on individual subject performance. Since different subjects were used for different caffeine doses in Gum 2 data, the individual models identified from Gum 2 data are excluded from further analysis.

Based on the individualized caffeine models identified from Gum 3 data, the response of these dose-dependent models to a single 100 mg caffeine input can be calculated for each subject (see Figure 6.73). Figure 6.74 shows the statistical response among eight low caffeine users from dose-dependent (100, 200 and 300 mg) individualized low-user models. Figure 6.75 shows the statistical response among six high caffeine users from individualized high-user models. As explained in section 2, a higher value of lapses shown in this caffeine-only response data indicates higher alertness. The results show that for both low and high caffeine users, the individualized model identified from 100 mg test data has statistically higher alertness as compared to the response of the identified 200 mg or 300 mg model.

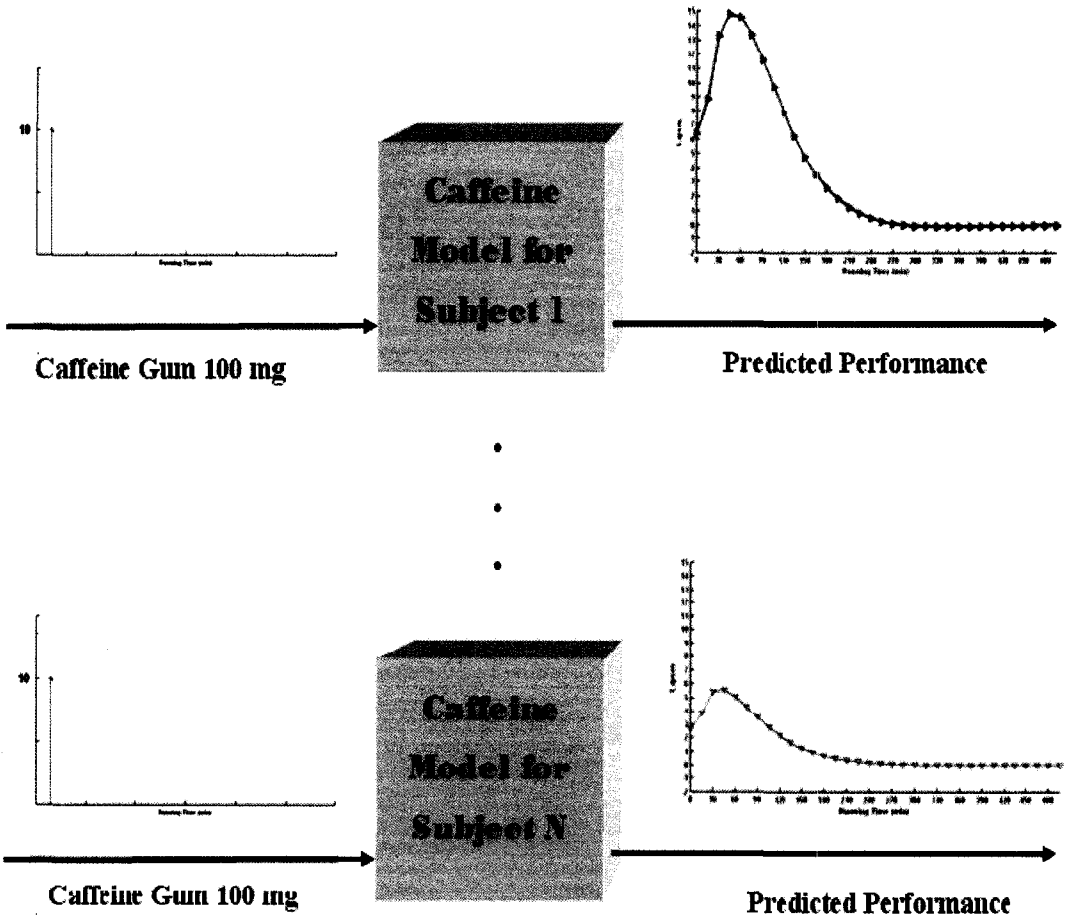

Figure 6.73: Individualized Performance Prediction Using One Caffeine Dose

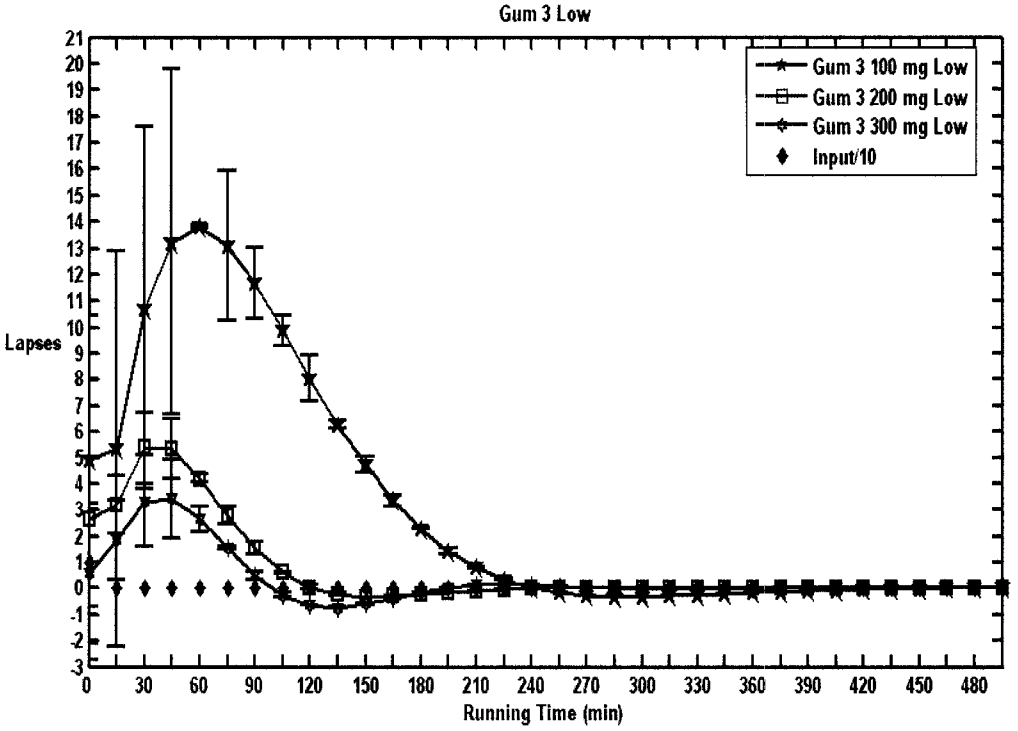

Figure 6.74: Statistical response of individualized dose-dependent models to a single 100 mg caffeine input for eight Gum 3 low-users.

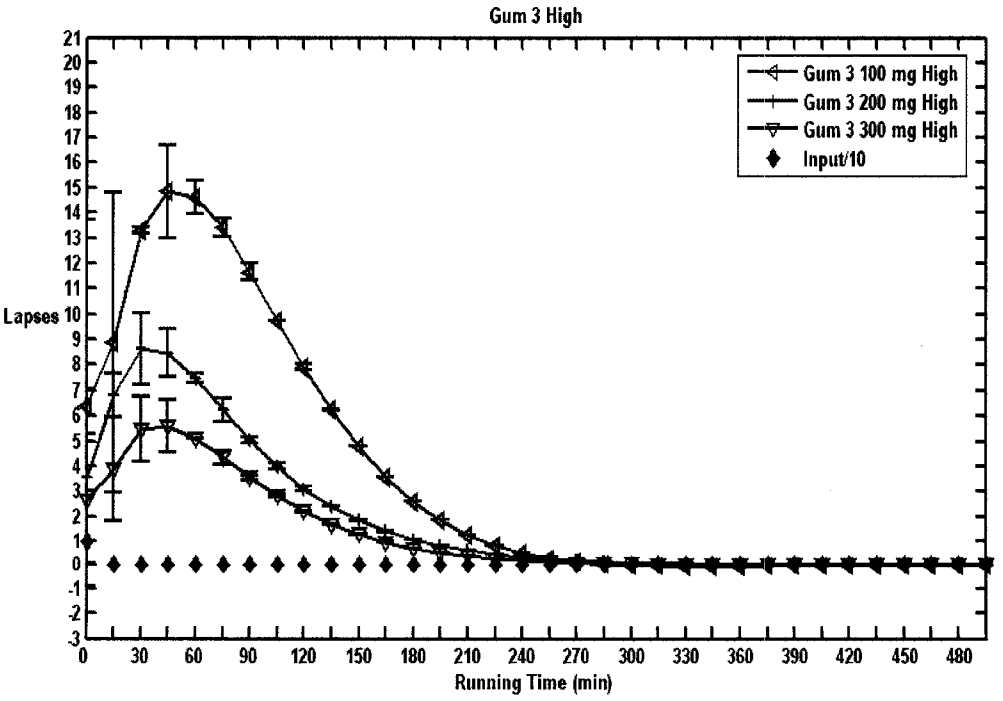

Figure 6.75: Statistical response of individualized dose-dependent models to a single 100 mg caffeine input for six Gum 3 high-users.

6.3 Effect of Habitual Caffeine Usage on Individual Subject Performance

Based on the individualized caffeine models identified from Gum 3 data, the response of these models to a single 100 mg dose input can be calculated for each subject. Figure 6.76 shows the statistical response of individualized 100 mg models to a single 100 mg dose input for eight low caffeine users as compared to six high caffeine users. The statistical response of individualized 200 mg and 300 mg models is shown in Figure 6.77 and 6.78, respectively. The results show that both low and high caffeine users have comparable responses based on 100 mg models. However, the response of either the 200 mg or 300 mg model shows that high caffeine users have a statistically higher response than low caffeine users.

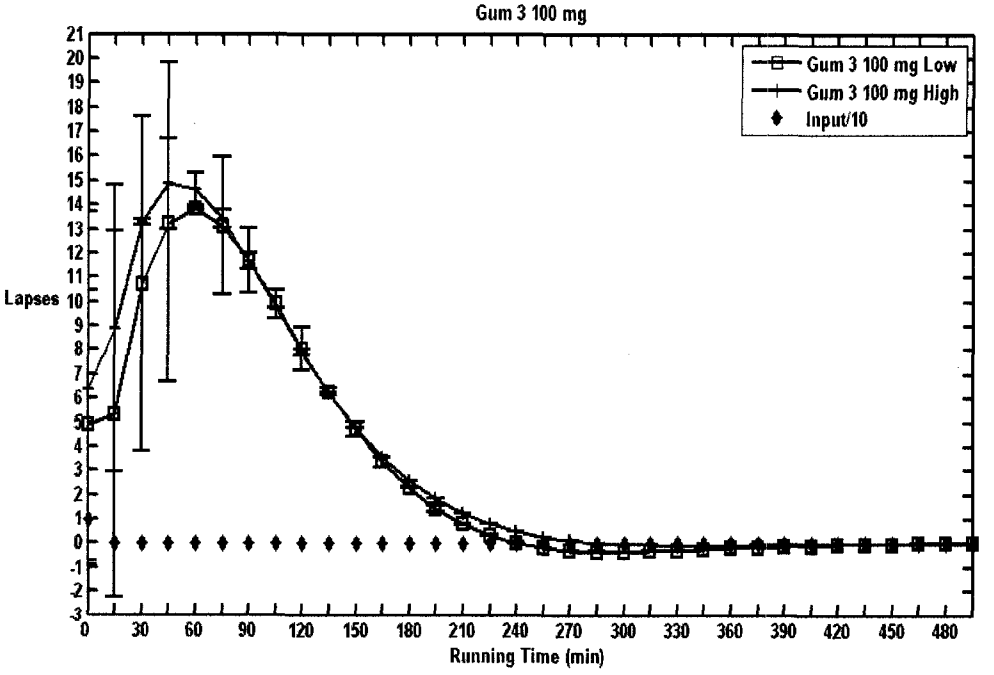

Figure 6.76: Statistical response of individualized 100 mg models to a single 100 mg input for eight low caffeine users as compared to six high caffeine users.

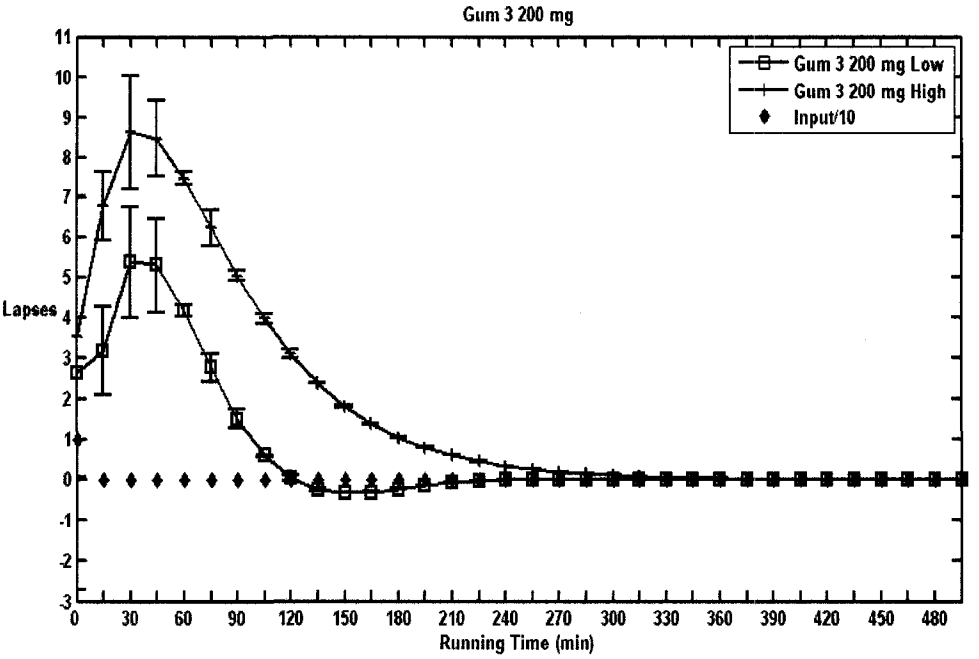

Figure 6.77: Statistical response of individualized 200 mg models to a single 100 mg input for eight low caffeine users as compared to six high caffeine users.

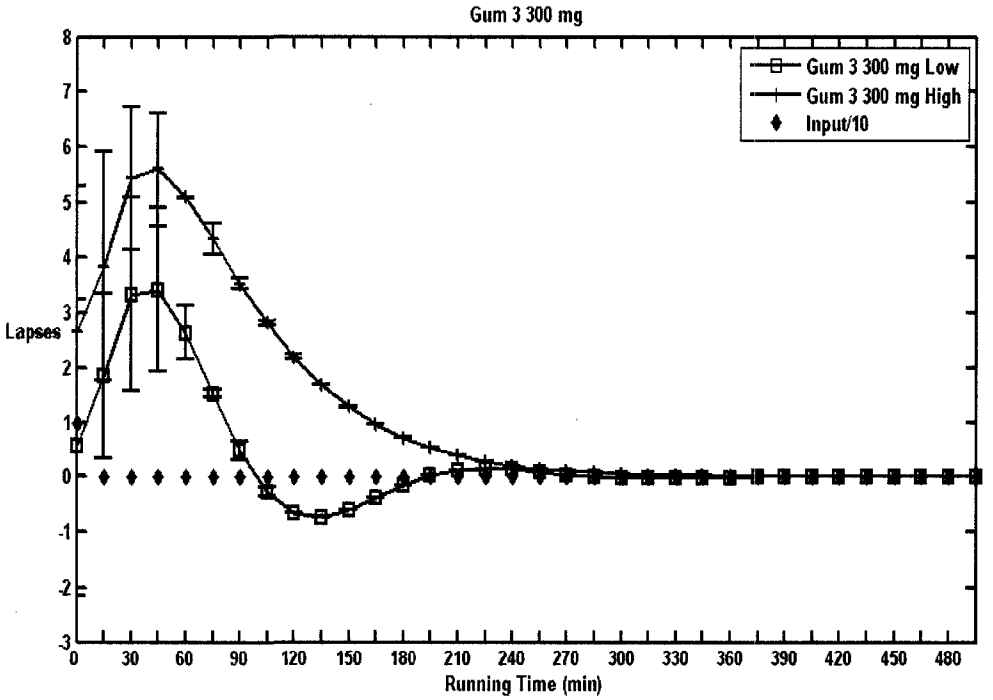

Figure 6.78: Statistical response of individualized 300 mg models to a single 100 mg input for eight low caffeine users as compared to six high caffeine users.

CHAPTER 7

CAFFEINE MODEL PREDICTION

In this chapter, we study how the identified model for one caffeine dose can be used to predict the caffeine effects for other caffeine doses. For a demonstration, the caffeine model identified from Gum 3 200 mg high-user population averages is selected to predict the caffeine effects of other caffeine doses. The results are shown in Figures 7.1 and 7.2. It is clear that the lower 100 mg caffeine dose is much more effective than the 200 mg model predicts. A higher 300 mg caffeine dose is less effective than the 200 mg model predicts. Moreover, the caffeine model identified from Gum 3 200 mg low-user population averages is selected to predict the caffeine effects for Gum 3 100 and 300 mg low-user. The results are shown in Figures 7.3 and 7.4. It is clear that the lower 100 mg caffeine dose is much more effective than the 200 mg model predicts. A higher caffeine dose of 300 mg is less effective than the 200 mg model predicts. In addition, the caffeine model identified from Gum 2 100 mg high-user population averages is selected to predict the caffeine effects for Gum 2 50 and 200. The results are shown in Figures 7.5 and 7.6. It is obvious that the lower 50 mg caffeine dose is much more effective than the 100 mg model predicts. A higher 200 mg caffeine dose is less effective than the 100 mg model predicts. In section 6.2, it is also found that the individual model identified from the 100 mg test data set a has statistically higher caffeine response as compared to the response of the identified 200 mg or 300 mg model. A similar result was found by Kaplan (Kaplan et al., 1997).

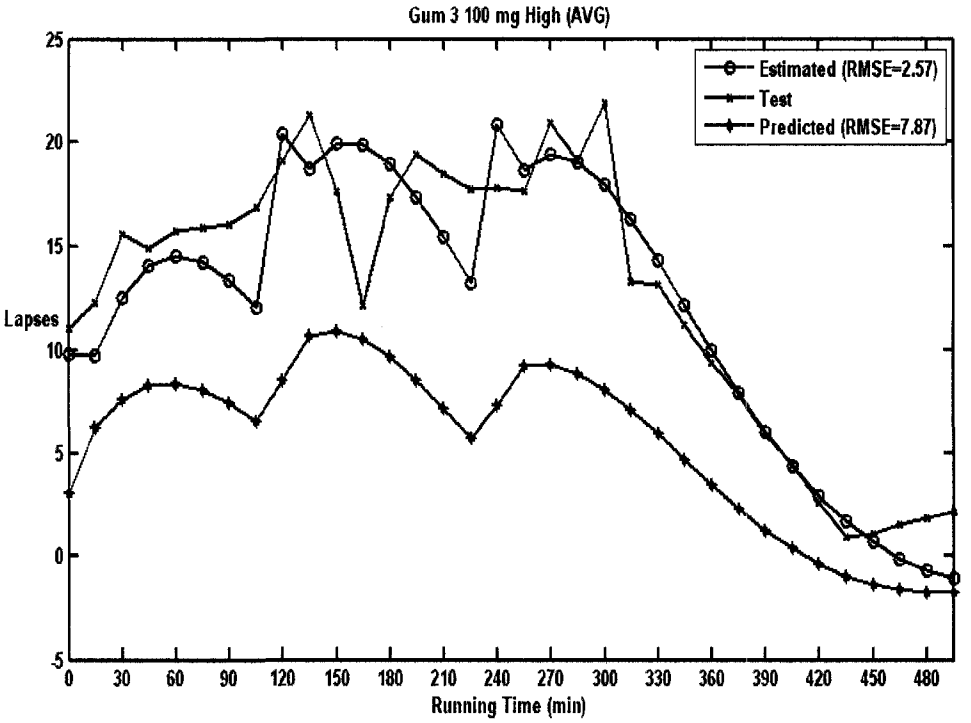

Figure 7.1: Prediction of 100 mg caffeine effect using 200 mg model for high-users based on population average data.

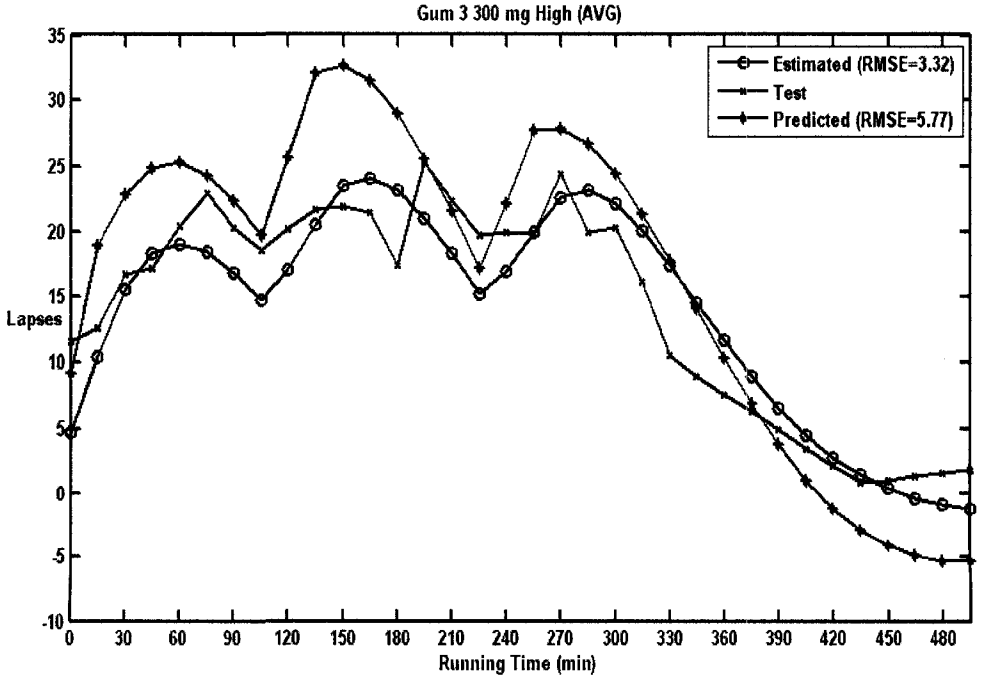

Figure 7.2: Prediction of 300 mg caffeine effect using 200 mg model for high-users based on population average data.

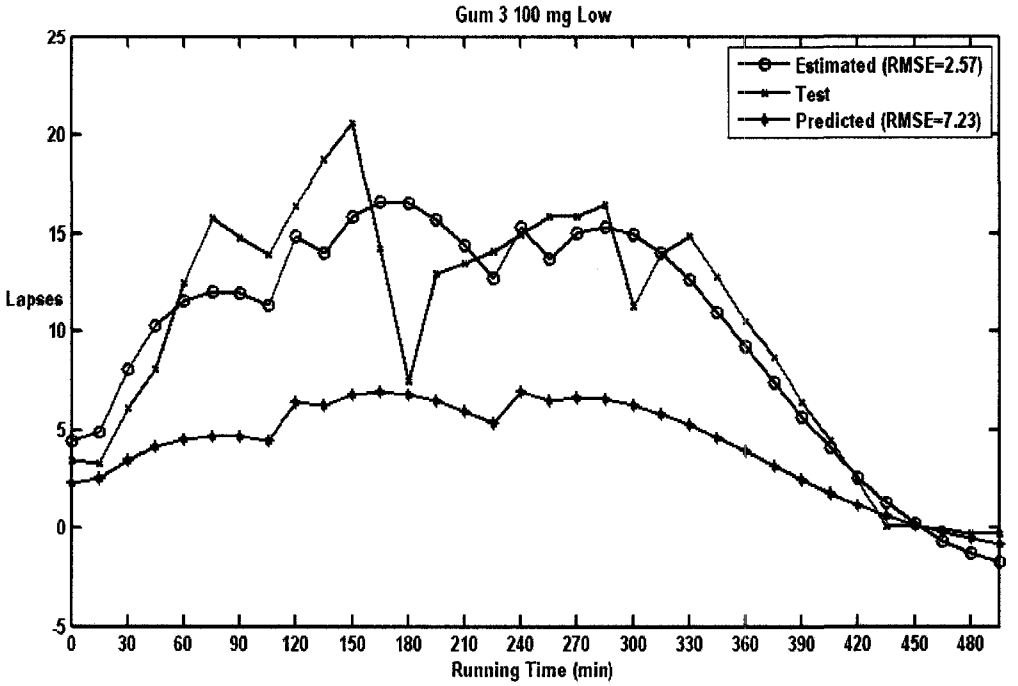

Figure 7.3: Prediction of 100 mg caffeine effect using 200 mg model for low-users based on population average data.

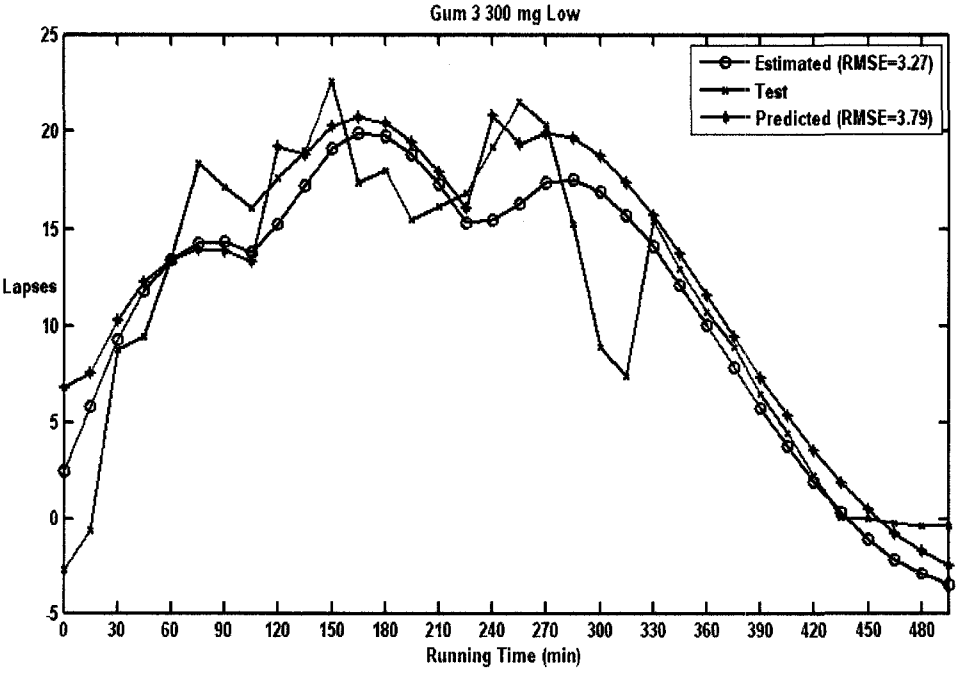

Figure 7.4: Prediction of 300 mg caffeine effect using 200 mg model for low-users based on population average data.

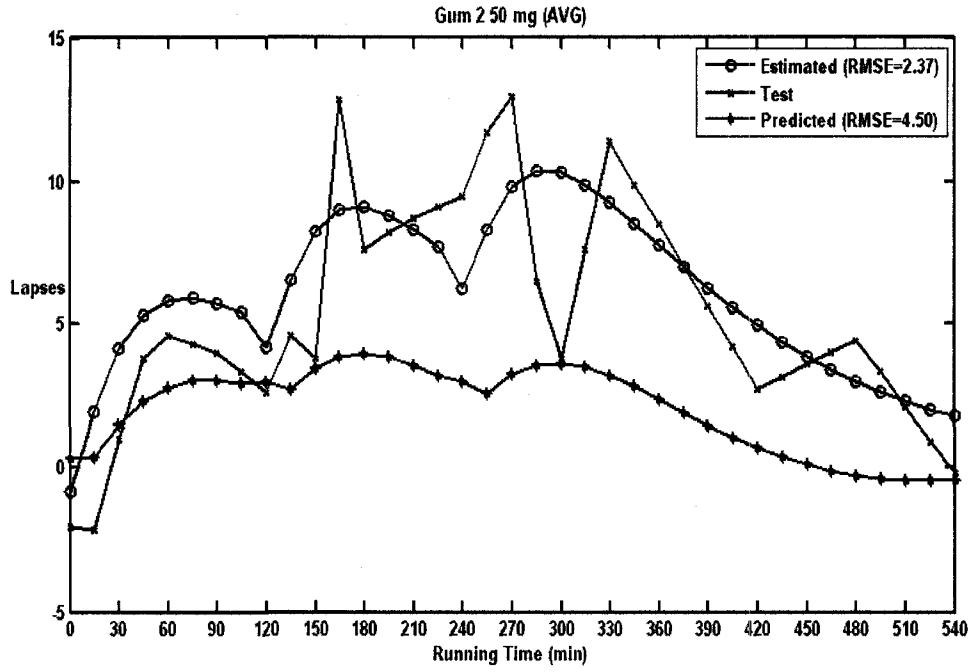

Figure 7.5: Prediction of 50 mg caffeine effect using 100 mg model for Gum 2 based on population average data.

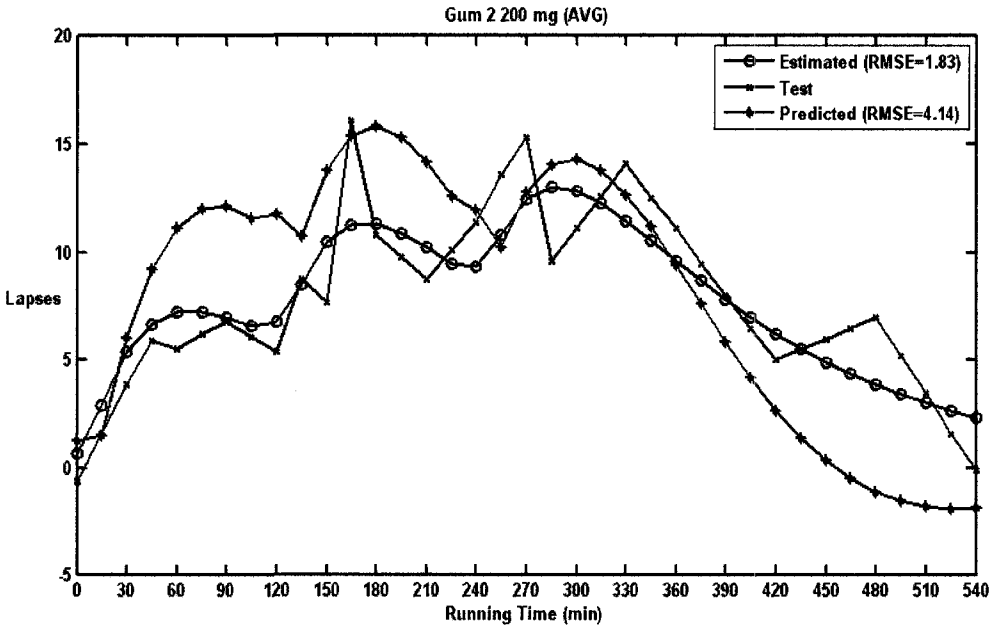

Figure 7.6: Prediction of 200 mg caffeine effect using 100 mg model for Gum 2 based on population average data.

To improve model prediction, a dose factor K is introduced as the scale factor for the input dose level. As shown in Figure 7.7, the state-space caffeine model used for prediction is modified as:

$$\begin{aligned} x(k+1) &= \mathbf{A}x(k) + \mathbf{B}K\mathbf{u}(k) \\ \mathbf{y}(k) &= \mathbf{C}x(k) + \mathbf{D}K\mathbf{u}(k) \end{aligned} \qquad (7.1)$$

The optimal dose factor K for Gum 3 high-user 100 mg and 300 mg can be obtained by minimizing the root mean squared error for the prediction. The improved prediction using the 200 mg high-user model with the optimal dose factor for the 100 and 300 mg dose is shown in Figures 7.8 and 7.9, respectively.

The optimal dose factor K for Gum 3 low-user 100 mg and 300 mg can be obtained by minimizing the root mean squared error for the prediction. The improved prediction using 200 mg low-user model with the optimal dose factor for 100 and 300 mg doses is shown in Figures 7.10 and 7.11, respectively.

The optimal dose factor K for Gum 2 50 mg and 200 mg can be obtained by minimizing the root mean squared error for the prediction. The improved prediction using 100 mg model with the optimal dose factor for the 50 and 200 mg doses is shown in Figures 7.12 and 7.13, respectively.

The use of dose factor to improve model prediction is also applied to all population averages and individualized models in Figure 7.14 and 7.15. Figure 7.15 shows that the dose factor is higher at low caffeine dose (100 mg) and lower at high caffeine dose (300 mg). However, there is no significant difference between high and low caffeine users.

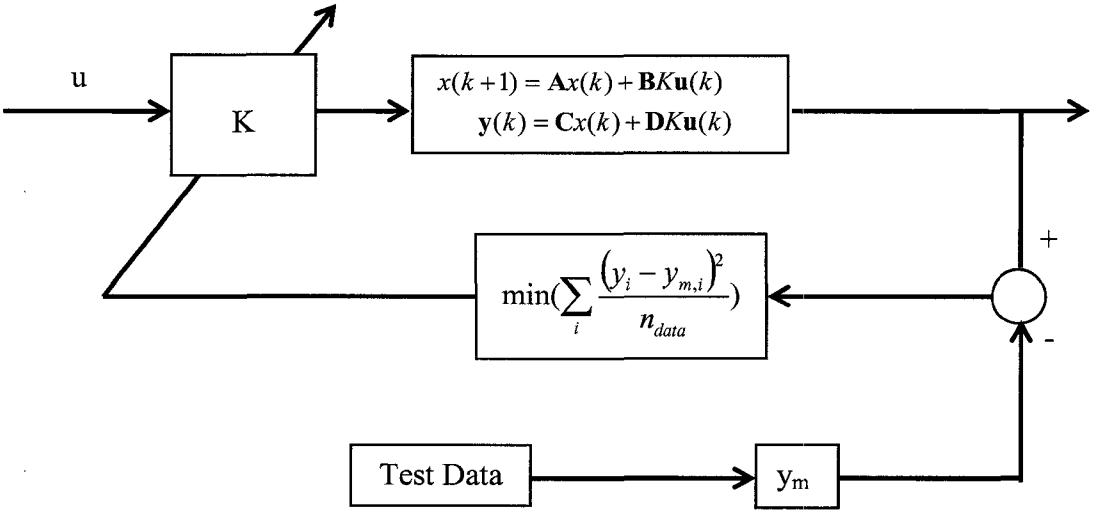

Figure 7.7: Use of dose factor K to adjust input caffeine level for model prediction.

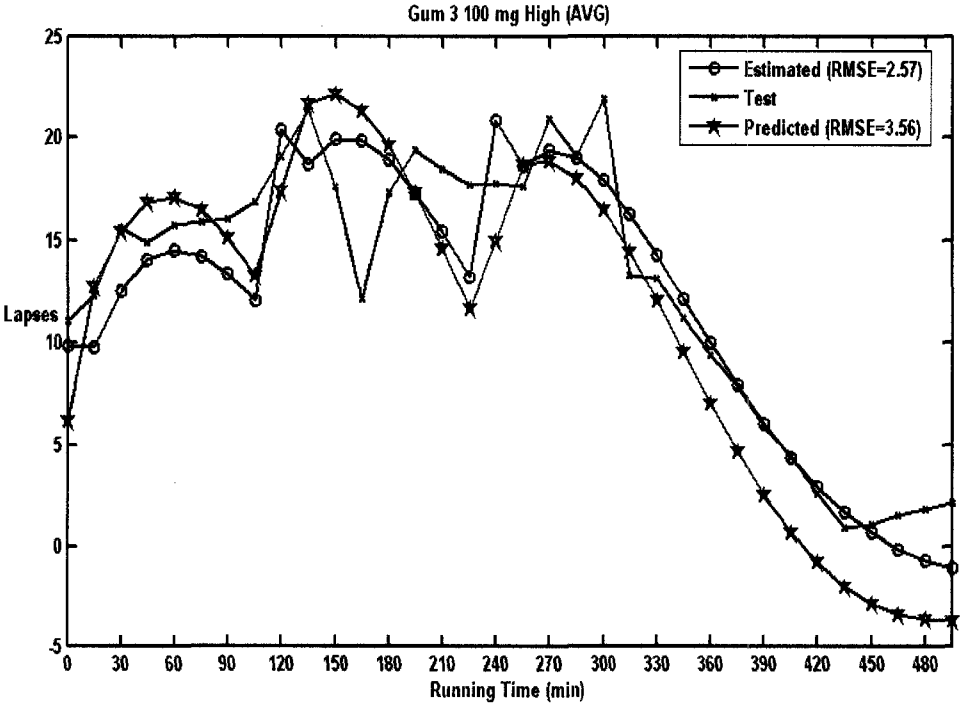

Figure 7.8: Prediction of 100 mg caffeine effect using 200 mg model and an optimal dose factor for high-users based on population average data.

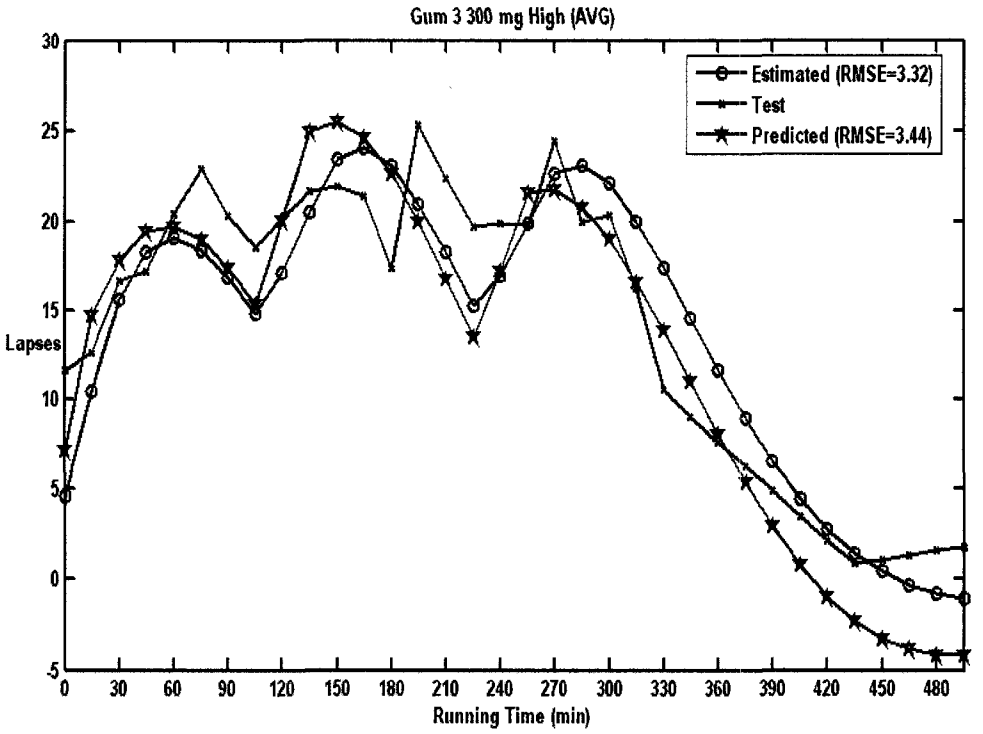

Figure 7.9: Prediction of 300 mg caffeine effect using 200 mg model and an optimal dose factor for high-users based on population average data.

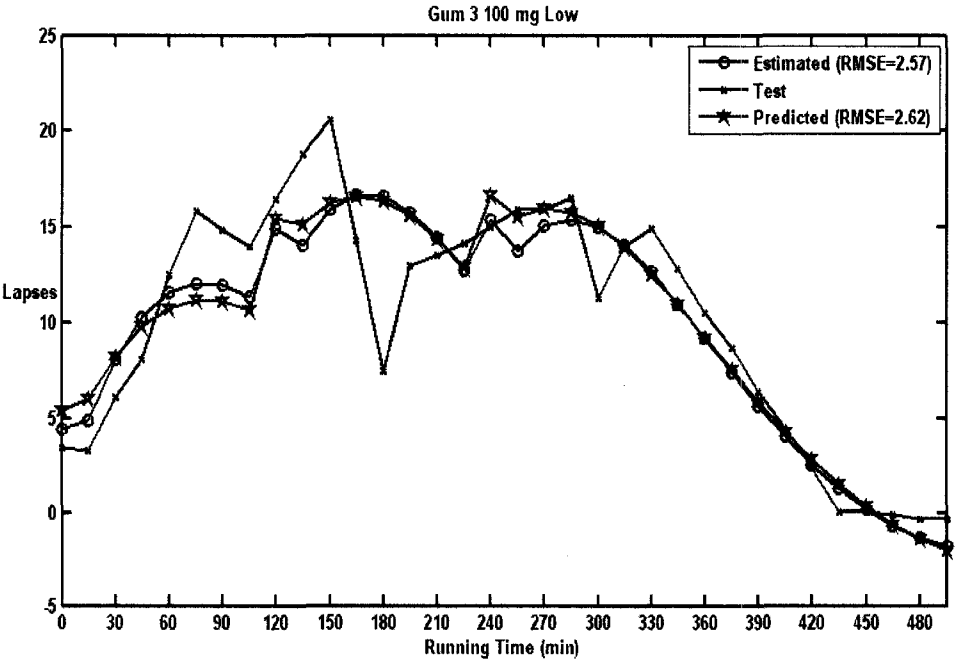

Figure 7.10: Prediction of 100 mg caffeine effect using 200 mg model and an optimal dose factor for low-users based on population average data.

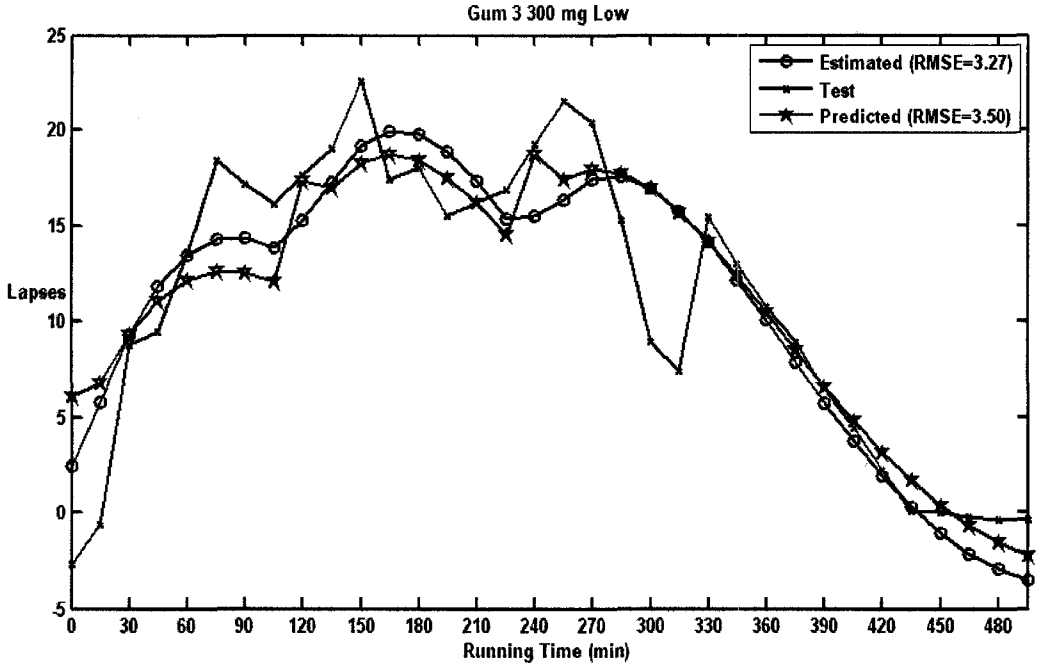

Figure 7.11: Prediction of 300 mg caffeine effect using 200 mg model and an optimal dose factor for low-users based on population average data.

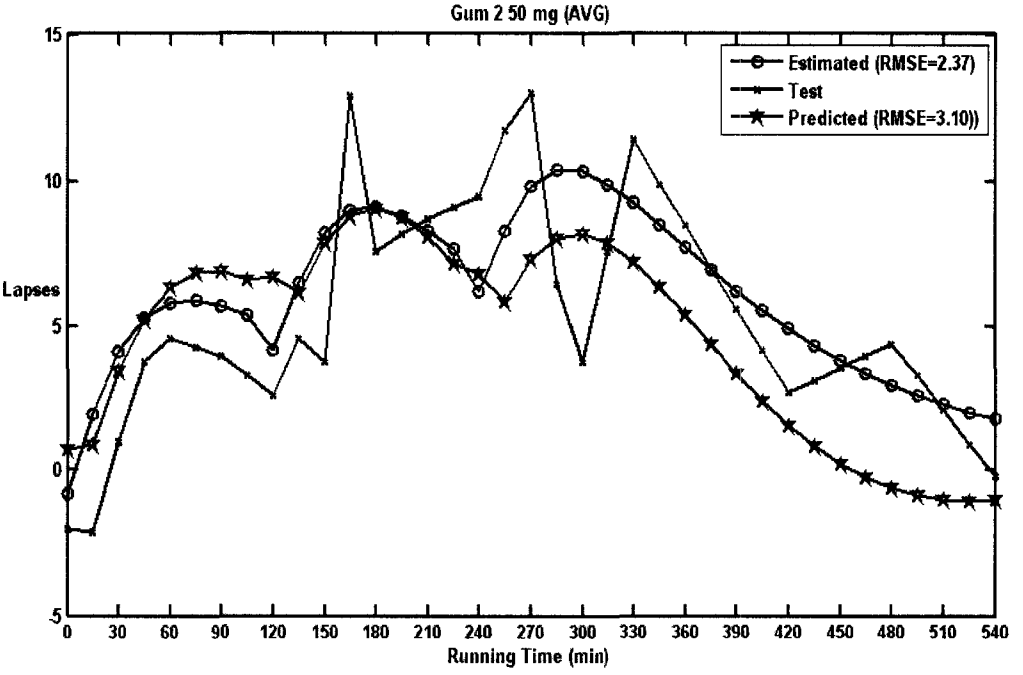

Figure 7.12: Prediction of 50 mg caffeine effect using 100 mg model and an optimal dose factor for Gum 2 on population average data.

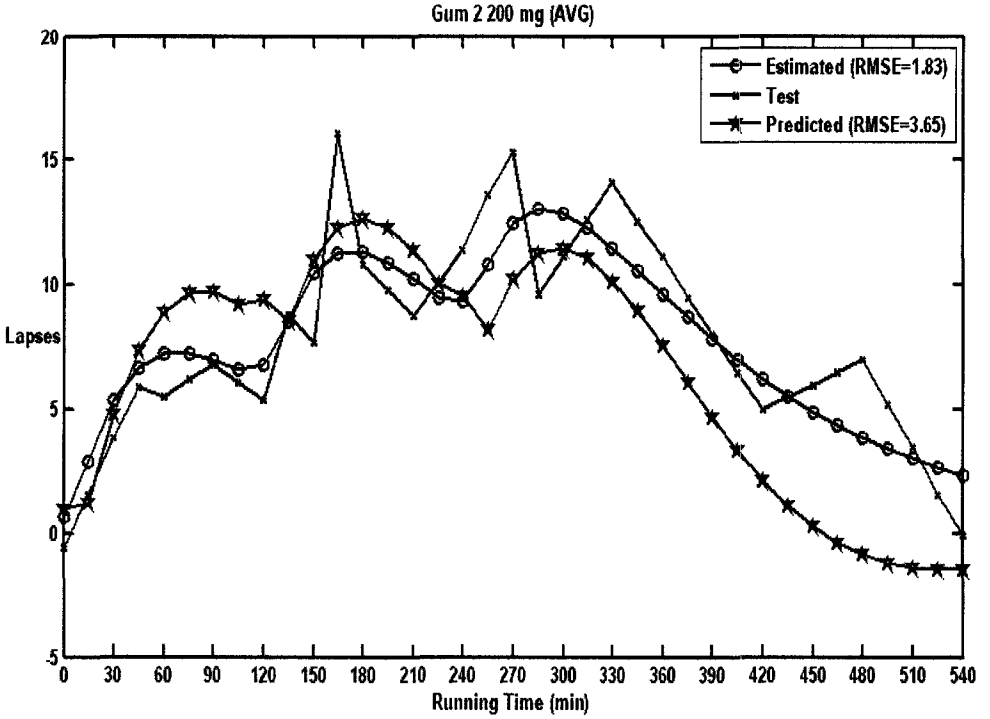

Figure 7.13: Prediction of 200 mg caffeine effect using 100 mg model and an optimal dose factor for Gum 2 on population average data.

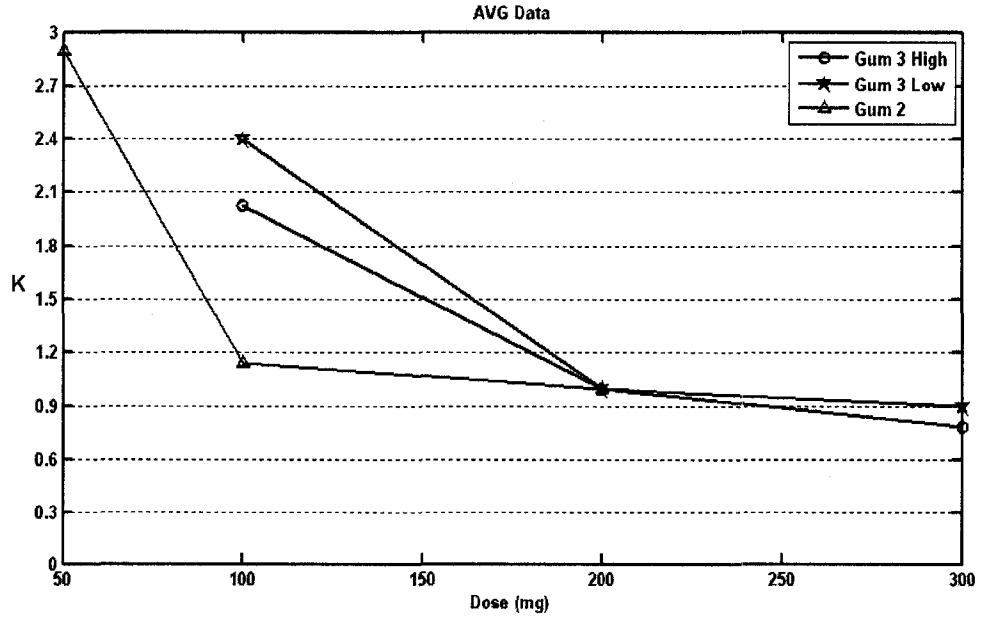

Figure 7.14: Optimal dose factor K vs. caffeine level for Gum 2 and Gum 3 based on population average data.

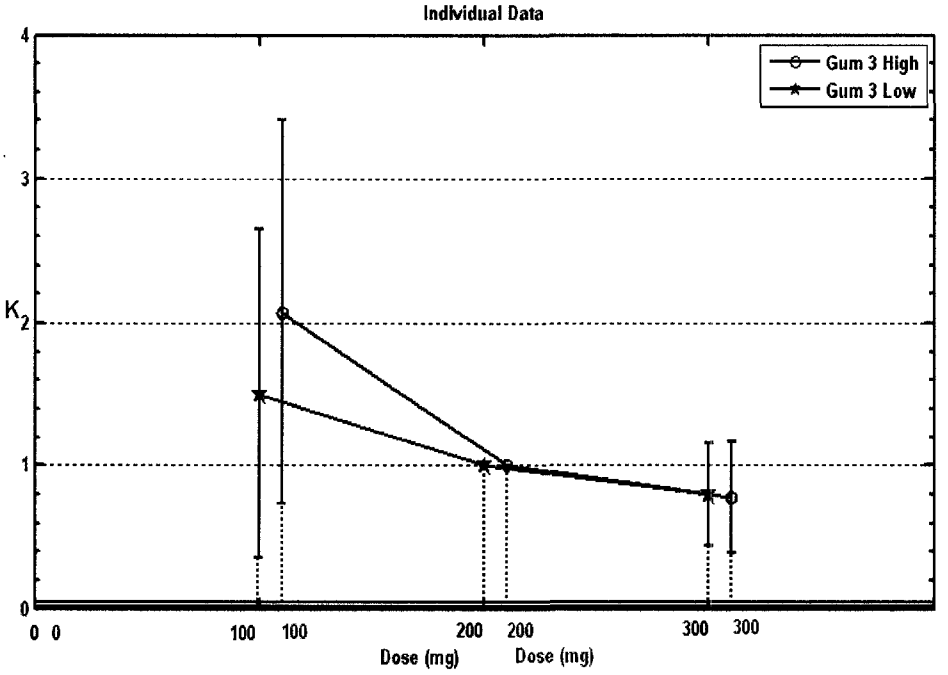

Figure 7.15: Optimal dose factor K vs. caffeine level for Gum 3 individualized models.

CHAPTER 8

CONCLUSIONS

8.1 Overview

In this study, the following caffeine model is proposed:

$$x(k+1) = Ax(k) + Bu(k), \quad y(k) = Cx(k) + Du(k)$$

$$\mathrm{A} = \begin{bmatrix} 0 & 1 \\ -a_2 & -a_1 \end{bmatrix}, \ \mathrm{B} = \begin{bmatrix} 0 \\ 1 \end{bmatrix}, \ \mathrm{C} = \begin{bmatrix} c_1 & c_2 \end{bmatrix}, \ \mathrm{D} = d_0 \tag{8.1}$$

This second-order state-space model in controllable canonical form can be easily merged into a two-process model with circadian and homeostatic effects for future study. In this caffeine model, five system parameters $[a_1, a_2, c_1, c_2, d_0]$ can be identified by using the proposed Observer/Kalman filter identification (OKID) algorithm. Identification of individualized caffeine model shows that the first two coefficients $[a_1, a_2]$ have small variations for both low and high caffeine users among all doses. This indicates that the caffeine dosage and habitual usage do not have much impact on the individualized caffeine model dynamics.

Based on the individualized caffeine models identified from Gum 3 data, the 100 mg model has a statistically higher caffeine response as compared to the response of the 200 mg or 300 mg models. The result also shows that both low and high caffeine users have

comparable responses based on the 100 mg model. However, the responses of the 200 mg or 300 mg models show that high caffeine users have statistically higher responses to caffeine.

Finally, it is shown that the proposed individualized caffeine model can be modified by adding a dose factor to the input of the model to improve the prediction for the performance of other caffeine doses.

8.2 Areas for Future Work

The research will be extended in one-step ahead prediction by using the same test data as studied for prospective study since the identified caffeine models can be used for prediction of future performance. The second-order state-space model in controllable canonical form can be easily merged into a two-process model with circadian and homeostatic effects. Therefore, the future work will be integrated into the dynamic two-process model of human performance, and then adapt the estimation and forecasting algorithm for the new, larger model. The first step will be to transform the caffeine model so that its structure is described in the form of a nonlinear state space model, as required by the Bayesian forecasting algorithm. Furthermore, future work will also integrate the caffeine parameters into the existing two-process model to create a single integrated model. At this point, the work will be given a fatigue and performance model that has a sleep/wake input, a chronic sleep restriction parameter and a caffeine input with associated caffeine parameters. Eventually, the estimation algorithm will be reconfigured for use with the expanded model, by introducing a new caffeine input to specify timing

and quantity of doses, redesigning the algorithm for the expanded number of states and inputs, and then selecting new tuning parameters for process covariances.

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APPENDIX A

SINGLE TRIAL CAFFEINE DOSES

Definition A1 (Gum 2) Laboratory-based conducted by the Division of Neuropsychiatry, Walter Reed Army Institute of Research, involving a range of multiple caffeine doses (three repeated doses of 0mg, 50mg, 100mg, or 200mg) during one night total sleep deprivation.

Description of protocol:

(a) 1 baseline day of 8 hours TIB (23:00 to 7:00).

(b) 1 night of total sleep deprivation with three repeated caffeine dosages administered at 2 hour intervals to four experimental groups.

Definition A2 (Gum 2 0mg) Placebo administered at 03:00, 05:00 and 07:00.

Definition A3 (Gum 2 50mg) 50mg dosage administered at 03:00, 05:00 and 07:00.

Definition A4 (Gum 2 100mg) 100mg dosage administered at 03:00, 05:00 and 07:00.

Definition A5 (Gum 2 200mg) 200mg dosage administered at 03:00, 05:00 and 07:00.

APPENDIX B

REPEATED TRIAL CAFFEINE DOSES

Definition B1 (Gum 3) Laboratory-based conducted by the Division of Neuropsychiatry, Walter Reed Army Institute of Research, involving a range of multiple caffeine doses (three repeated doses of 0mg, 50mg, 100mg, or 200mg) during one night total sleep deprivation. Two groups participated, low users of caffeine and high users. Each subject will complete four separate trials with a minimum of four weeks between trials.

Description of protocol:

(a) 1 baseline day of 8 hours TIB (23:00 to 7:00).

(b) 1 night of total sleep with repeated caffeine dosages to low users of caffeine and high users. Participants completed four separate trials with a minimum of four weeks between trials. At each trial subjects were given three repeated doses of caffeine (0mg, 100mg, 200mg, or 300mg) at two hour intervals.

Definition B2 (Gum 3 Low 0mg) Placebo administered at 03:00, 05:00 and 07:00.

Definition B3 (Gum 3 Low 100mg) 100mg dosage administered at 03:00, 05:00 and 07:00.

Definition B4 (Gum 3 Low 200mg) 200mg dosage administered at 03:00, 05:00 and 07:00.

Definition B5 (Gum 3 Low 300mg) 300mg dosage administered at 03:00, 05:00 and 07:00.

Definition B6 (Gum 3 High 0mg) Placebo administered at 03:00, 05:00 and 07:00.

Definition B7 (Gum 3 High 100mg) 100mg dosage administered at 03:00, 05:00 and 07:00.

Definition B8 (Gum 3 High 200mg) 200mg dosage administered at 03:00, 05:00 and 07:00.

Definition B9 (Gum 3 High 300mg) 300mg dosage administered at 03:00, 05:00 and 07:00.

VITA

Chun-Hui Huang was born in Kaohsiung, Taiwan. He received his B.S. degree in Electrical Engineering from Da-Yeh University in 1999 and M.S. degree in Computer Science from University of Detroit Mercy in 2003.

From December 2002 to December 2003 he was a laboratory assistant at University of Detroit Mercy. In 2004, he worked as a field application senior engineer for Behavior Tech Computer Corp in Taiwan and was responsible for passing account specifications and needs. From May 2005 to May 2008 he was a research and teaching assistant at Old Dominion University.

He was invited to publish a chapter in *Methods in Enzymology.*

He currently lives in Norfolk, Virginia, with his wife, Migo, and daughter, Phoebe.

He attributes all his successes to the Lord and desires to glorify Him in all his endeavors.